August 10, 2019 **BY EMAIL**

SUBJECT:
PATENT SYSTEM IS OBSTRUCTING ADVANCEMENT IN NUTRITION, KEEPING PUBLIC ON DRUGS AND DEVICES, AND PROMOTING THE NATIONAL DISEASE BURDEN AND HEALTH CARE COSTS

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Subject Recap:
Patent System is Obstructing Advancement in Nutrition, Keeping Public on Drugs and Devices, and Promoting the National Disease Burden and Health Care Costs

Case in Point:
The Disdainful Treatment of Asha Nutrition Sciences' Patent Applications (12/426,034 (pending since 2009), 13/332,251 (granted after 8 years of pendency), and 13/877,847 (pending since 2013)) by the United States Patent and Trademark Office, and the United States Court of Appeals for the Federal Circuit, and The Worldwide Consequences of the Same

Dear Mr. President, Madam Speaker, Honorable Congress Members:

We the public and the United States Government have rallied, caucused, campaigned, complained, and grumbled about our over $3 trillion annual healthcare costs and associated social burden. Rather it is a national obsession to lament about the health care system. Yet when our small company, Asha Nutrition Sciences, in 2008 presented the Government (USPTO) with an innovative inexpensive solution to significantly solve the problem at the base via tailored lipid nutrition (a fitting complement to Government sponsored healthcare), it was snubbed by the Government (USPTO, the US Court of Appeals for the Federal Circuit, and the US Supreme Court) rather apathetically, and the Government declined to grant us proper and timely patent rights to properly nurture the innovation to bring about leaps of advancement for future generations.

The legislature does not restrict patent grant to nutritional innovations, but in practice the patent system disfavors such patent grants, and when nutritional patents are granted, they are severely restricted or dragged in prosecution robbing off proper scope and term for effective implementation, *neutering* the innovation. *Tragically if our innovations were drawn to drug candidates similarly differentiated over prior art, the patents would have been granted many years ago*. Narrow patents in the nutrition arts and favorable patent grant to drugs have created *patent-practice-made humanitarian crises* by perpetuating misinformation, taking us farther away from solving nutritional problems and sustainability, fostering stagnation in the nutrition art, and making us dependent on drugs and devices.

Of note is the disdainful treatment of our patent applications, particularly the application no. 12/426,034 by the US Government and its worldwide effects. We request you to intervene in this *extraordinary case and abrogate the holdings of the USPTO and the Federal Circuit that mutilate Title 35 of the United States Code*.

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ANNEXES[1]:

[1] Almost all the references/publication cited in this paper are on record at USPTO and have been submitted to the Federal Circuit, with the exception of petitions and briefs submitted to the Supreme Court, which were added to the record at the USPTO but not at the Federal Circuit. For the sake of brevity, only a subset of documents from the Joint Appendix submitted to the Federal Circuit is included here, additional documents are available upon request.

I. Prosecution Summary of the '034 Application

Application no. 12/426,034 (the '034 application (Annex A)) was filed on April 17, 2009 and has April 2008 priority. The inventions pertain to tailored delivery of dosages of omega-6 fatty acids relative to other lipids (fatty acids, antioxidants, and phytochemicals), because of continuing *mass miseducation in the art that omega-6 fatty acids are unhealthy* and that intake and activity of omega-6 should be suppressed using other nutrients, and grave consequences of this mass miseducation on public health.

Due to its bias against nutrition the USPTO issued a dozen improper rejections, citing remotely related art as anticipatory under 35 USC § 102 and applying obviousness rejections under 35 USC § 103 despite opposite teachings in the prior art. None of the rejections could not be sustained. The obviousness rejections were particularly improper since the '034 Application itself evidences that the subject matter is poorly understood, that there are opposite teachings in the prior art, and that the long-felt critical public health need remains unmet (e.g., see Annex A paragraphs [0006]-[0007]). Furthermore, even the art cited by the USPTO teaches the opposite of the claimed subject matter (discussed below).

However, then the USPTO resorted to *excising limitations* from the claims, *mutilating* the law, and *reconstructing* the prior art and products of nature to allege anticipation by nature under § 101—applied for the first time in *7th* Office Action in October 2013. The Examiner issued final rejection on September 22, 2015, ***rejecting all 55 claims[2] under § 101*** over alleged anticipation by *alleged* "products of nature", *individual oils*, olive oil (Annex B) and walnut oil (Annex C), each separately, and ***rejecting 52 claims (except Claims 102, 107, and 119) under § 102*** over alleged anticipation by *individual fruits/nuts*, olives (Annex D) and walnuts (Annex E), each separately.

Some claims were also rejected over alleged anticipation by U.S. Patent No. 5,549,905 ("Mark") (Annex F). Applicant[3] submitted reams of arguments and evidence including skilled person's testimony that Mark does not anticipate, however, Mark is not dispositive in any case since most claims (e.g. independent Claim 91 and dependent claims, and dependent claim 82 which can replace claim 65) are not rejected under Mark.

Patent Trial and Appeal Board affirmed Examiner's rejections on April 15, 2016 (Annex G) and denied Rehearing on June 21, 2016.

[2] See full claim chapter of the rejected claims at the end of Annex A.
[3] "Applicant" refers to Asha Nutrition Sciences, the assignee of the application, and "inventor" and "I" refers to Urvashi Bhagat, the undersigned throughout this paper.

Independent Claim 65 rejected under § 101 (allegedly anticipated by olive oil) and under § 102 (allegedly anticipated by olives) recites:

A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids from different sources, and wherein

(1) omega-6 fatty acids are 4-75% by weight of total lipids and omega-3 fatty acids are 0.1-30% by weight of total lipids; or

(2) omega-6 fatty acids are not more than 40 grams.

Dependent Claim 102 *solely* rejected under § 101 (i.e., not anticipated by any product of nature, including olives or walnuts or their oils but allegedly still a product of nature because it is obtained by mixing naturally occurring omega-6, omega-3, and omega-9 fatty acids) recites:

The formulation of claim 65, wherein the dosage of total fat is 10-100 grams, the dosage of omega-6 fatty acids is from 1 to 40 grams; the dosage of omega-3 fatty acids is from 0.1 to 5 grams, the ratio of monounsaturated fatty acids to polyunsaturated fatty acids is in the range of 1:1 to 3:1, the ratio of monounsaturated fatty acids to saturated fatty acids is 1:1 to 5:1, the ratio of omega-9 to omega-6 fatty acids is in the range of 1:1-3:1, and the ratio of omega-6 to omega-3 fatty acids is in the range of 4:1 to 45:1.

Independent Claim 91 rejected under § 101 (allegedly anticipated by walnut oil) and under § 102 (allegedly anticipated by walnuts) recites:

A lipid-containing formulation, comprising a dosage of omega-6 fatty acids, wherein the omega-6 fatty acids are greater than 20% by weight of the total lipids, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids from different sources, the formulation comprising polyunsaturated, monounsaturated, and saturated fatty acids, and wherein the formulation includes at least

(i) one or more polyunsaturated fatty acids selected from [omitted], and

(ii)nutrients including at least

(a) one or more polyphenols, or

(b) one or more phytochemicals,

the one or more phytochemicals being selected from [omitted].

Thus, USPTO obstructed *critical innovation* directed to specific *formulations* comprising *intermixtures in casings* and *dosages of lipids*—*that is "composition of matter" and "manufacture" and "process*"—over individual foods contrary to 35 USC § 101. Critical does not mean unpatentable or "product of nature;" further, nature being highly unpredictable in nutrient (lipid) content is incapable of providing "dosage" of anything, let alone tailor it for subjects (discussed below).

Further, § 102 was applied though *identical* invention as claimed is not disclosed and enabled in either of olives, walnuts, or their oils, or Mark, and a competitor could *not* obtain the claimed subject matter from the prior art and that the prior art does *not necessarily* function as claimed. Congress created § 103 in the 1952 Patent Act for such rejections, but USPTO applied the rejections under § 102 because § 103 rejections could not be sustained due to unexpected results and opposite teachings in the prior art, i.e. USPTO circumvented the law. The impropriety of the rejections is discussed further in Sections III.5 and IV.1-2.

United States Court of Appeals for the Federal Circuit rubberstamped USPTO on March 16, 2018, contrary to Title 35 USC and a large body of its own and Supreme Court precedents without a meaningful review, as required by Administrative Procedure Act, issuing a non-precedential opinion (Annex H) so as to not affect the case law ***singling out this case for injustice***, and denied the Petition for Rehearing and Hearing En Banc (Annex I) on June 1, 2018, heedless to the Amicus Brief submitted on May 9, 2018, and despite the opinions of well-known patent lawyers that the case was improperly decided (see Addendums to Annex I). Applicant submitted an Open Letter to Director Andrei Iancu at USPTO and Chief Judge Sharon Prost at the Federal Circuit, on April 27, 2018 asserting that USPTO's and the Federal Circuit's actions were improper (Annex J).

Petition for a Writ of Certiorari was submitted to the Supreme Court of the United States on August 29, 2018 (Annex K) (case no. 18-277) supported with an amicus brief submitted on October 5, 2018 (Annex L), and a Supplemental Brief on October 22, 2018 (Annex M). The Supreme Court denied the acceptance of the amicus brief for being one day late and the Petition on October 29, 2018.

In view of extreme abuse of discretion in examination and appeal review, Petition for a Writ of Mandamus was submitted to the Supreme Court on March 30, 2019 (Annex N) (case no. 18-1274). An amicus brief was submitted on May 3, 2019 (Annex O). The Supreme Court denied the Petition on May 13, 2019. Petition for Rehearing for Writ of Mandamus was submitted on June 7, 2019 (Annex P), which was denied on July 15, 2019.

In view of intervening circumstances in the form of the US Senate's recently-published proposed language to reform Title 35 U.S.C. § 101 based on problematic behavior of the USPTO and the lower courts[4], Petition for Rehearing for the Writ of Certiorari (case no. 18-277) was submitted to the Supreme Court on July 11, 2019 (Annex Q), which is currently pending.

[4] https://www.tillis.senate.gov/services/files/E8ED2188-DC15-4876-8F51-A03CF4A63E26

II. The Claimed Inexpensive Innovative Solution— *Formulations of Tailored Lipid Dosages!*

The claimed inexpensive innovative solution is *formulations of tailored lipid dosages*, particularly of omega-6 fatty acids—**more critical for health than milk at any age** and **more crucial for protecting and enhancing public health than the most effective healthcare plan**, whether we call it "universal health care", "Medicare for all", or by any other name, particularly in view of the mass chaos in the art.

Chronic diseases and preventable medical conditions cost about $3.7 trillion annually in the United States[5]. Almost all chronic diseases are associated with improper intake of lipids (fatty acids, certain vitamins like A, E, D, K, and certain phytochemicals like sterols and polyphenols) evidenced by 100s of studies conducted in past 100 years[6]. This is because lipids are crucial components of cell membranes in animal body and play critical role in many physiological functions. For example, they are involved in gene regulation, and their derivatives are important hormones and biological messengers, affecting functions such as blood vessel dilation, platelets aggregation, pain modulation, inflammation, and cell growth. Therefore, when lipid intake is corrected by delivery of tailored lipid dosages by subject type, the foundation of health is corrected, hormonal balance is corrected, and immunity is strengthened and susceptibility to infections is reduced.

Therefore, ***the claimed inventions can substantially reduce the suffering of 117 million Americans from chronic diseases and of 80% of women from hormonal issues*** and ***can complement Government sponsored healthcare.***

Americans are literally put under a knife in cardiovascular surgery and subjected to drugs and devices (treatments) in diabetes, because ***treatments are made more financially rewarding by preferentially giving them patents/exclusive markets***, and ***preventative solutions such as claimed tailored lipid dosages are denied patent protection and therefore effective implementation***. For example, why are we throwing medications on people who have mild depression or on young women suffering from premenstrual syndrome, which can be significantly abated with correct lipid delivery? Same with,

- 90 million people suffering from diabetes or pre-diabetes,
- 54 million people with arthritis,
- 26 million people with asthma, and so on...

If a business is paid $10,000 or like for treatments favored by the patent system, why would they provide lipid dosages for $100 or like? It is basic economics!

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[5] Milken Institute, **"**The Cost of Chronic Disease in the U.S.," May 2018.

[6] E.g., see Baum et al*., "Fatty acids in cardiovascular health and disease: A comprehensive update"* Journal of Clinical Lipidology (2012) 6, 216–234; Bhagat U. Das UN. "*Potential role of dietary lipids in the prophylaxis of some clinical conditions"* Arch Med Sci 2015; 11, 4: 807–818 (Annex Y).

However, when preventative solutions such as tailored lipid dosages are given patent protection, the limited exclusivity allows higher product margins and a protected period to recover investment in the required novel infrastructure for the novel product platform.

Ultimately, we all win by implementing such critical preventative solutions:

- when prevention is in full gear, we can reallocate resources (currently usurped in treatment) to find cure to ailments that cannot be prevented, potentially benefiting "treatment businesses";
- reduction in suffering from disease increases productivity and per capita income;
- reduction in suffering from disease increases productivity and Gross Domestic Product; and
- reduction in suffering from disease increases productivity and per capita income and in turn increases taxes earned by the Government.

Patents for Humanity Application was submitted to USPTO on November 8, 2015 (Annex R) asserting the importance of the innovation particularly for the impoverished populations. Additionally, *eleven* testimonies from esteemed scientists are on record testifying that the claimed solutions are extremely important for public health (a subset of which is included as Annexes S-X).

In his testimony of September 29, 2014 (Annex U), Dr. Rustagi testified: *"Thus, the art recognized in 1929 that the problem existed as noted in paragraph [0019]. However, the art has failed to solve the long-felt, critical and unmet need until the April 2008 priority date of the subject patent application, i.e. for ~80 years. There have been many persistent attempts as evidenced by the references cited above (e.g. Mark et al., whfoods.com, Lands 1986 and 2005; Simopoulos 1999; Hamazaki et al., 2003 supra), but the problem has not been solved. Lipid art has been struggling to find what are the right combinations of omega-6 and omega-3 and other lipids for consumption, how to keep the fatty acids stable on shelf (without formation of toxic compounds) but bio-available in-vivo (Chen and Chaiyasit supra). Inventions of instant claims 65, 91, 98, 122, 129, and 130 have devised the solutions. Thus, the invention of the subject patent application solves a long-felt critical persistent unmet need, and has great potential to protect and improve public health."* See para [0019]-[0023].

"[The technologies]… are well-reasoned and directed at much needed lipid solutions, particularly in light of mass erroneous teachings and confusion in the lipid art." See para [0026]."

Drs. Robert Rucker and Undurti Das have given similar testimony, which is on record at USPTO and was submitted to the Federal Circuit in the Joint Appendix.

III. Why Are Tailored Lipid Dosages Not Implemented Given the Momentous National Importance?

It is self-evident from our daily lives and the prosecution history at USPTO (discussed above and below) that the innovation described above has not been implemented despite the momentous national implications.

The reasons include:

1. Certain aspects of the science are not well understood.
2. Misconception that teaching and publication of tables listing lipid content in common foods is sufficient.
3. Tailored lipid dosages are difficult to implement.
4. Tailored lipid dosages are economically infeasible business without sufficient patent scope.
5. The patent system disfavors proper patent grant to nutritional solutions
6. Special interest groups including the patent system thwart preventative efforts.

Each of the above points is further elaborated below.

1. Certain Aspects of the Science are Not Well Understood

There is mass misinformation both in the popular and scientific media as to what constitutes proper lipid intake.

Prior to 2008 (the priority date of '034 application) scientists understood that lipids are important for health, but they failed to understand the relative importance of various lipid classes and total lipid intake. For example, prior to 2008, scientists overwhelmingly taught to reduce intake of omega-6 family of fatty acids and increase the intake of omega-3 family of fatty acids, because omega-6 was widely believed to cause inflammation and numerous diseases and omega-3 was believed to be anti-inflammatory and counter the effects omega-6[7]. Prior to 2008, low omega-6 to omega-3 ratios like 1:1 or 2:1 were widely taught and very low dosages, for example *less than 1g* (less than 1% of calories) were taught[8]. Moreover, whenever prior art found another nutrient that inhibited the activity of omega-6 fatty acids, they recommended increased intake of such a nutrient[9].

[7] Simopoulos et al., "Essentiality of and Recommended Dietary Intakes for Omega-6 and Omega-3 Fatty Acids" Ann Nutr Metab 1999;43:127–130 (Annex Z).
[8] *Lands WE. "Dietary Fat and Health: The Evidence and the Politics of Prevention"* Ann. N.Y. Acad. Sci. 1055: 179–192 (2005), (page 183, para 4) (Annex AA).
[9] Wu D. et al., Am J Physiol Cell Physiol 275:661-668, 1998; Shah et al., Biochemical Pharmacology, Vol. 58, pp. 1167–1172, 1999; O'Leary et al., Mutation Research 551 (2004) 245–254.

Such teachings were reported in numerous scientific publications, numerous patents were issued to high omega-3 containing formulations and methods of treatment[10], and many mainstream publications advocated high use of omega-3[11]. Many companies marketed and profited from such products containing high amounts of omega-3. For example, Lovaza (omega-3) was marketed by Reliant Pharmaceuticals (sold to GlaxoSmithKline for $1.6 billion in 2007).

In early 2000s, motivated by my own mother's suffering from neural disease and premature death, I investigated the effect of relative intake of various lipids in live subjects and was astonished to find that such a large body of scientists had been incorrect and that they had endangered public health at such a large scale[12]. I found dosage of omega-6 to be most important for health, dependent on age, gender, bodyweight (e.g., greater than 5% of calories, noting that % of calories is not synonymous with dosage) and that omega-3 requirement for health was very low and its benefits were ephemeral, that long-term effects of fatty acids were different from short-term, that ratios of omega-6 to omega-3 should be at least 4:1 and could be very high such as 50:1, that the dosage was the most important factor. For example, if we kept the dosage of omega-6 for an adult female below 20g/day, the ratio became less relevant, but that high relative amounts of omega-3 interfered with omega-6 actions. I also found that initial increase in omega-6 from deficient state caused unfavorable symptoms but that health improved after the body adjusted to higher dosage of omega-6.[13] This explained the prior art had failed to understand the dose-effect of omega-6.

Understanding the dose-effect was an important finding, which the prior art had failed to understand. The prior art held that there was a proportional increase in adverse health with step-wise increase in omega-6 in the range of 0.5 to 4.4% of calories[14], therefore "ingestion of about 1 percent of daily calories" or even "0.5-1.0% of calories"—0.9-1.9g/day based on 1700-calorie diet—met the omega-6 requirements[15].

However, my experiments demonstrated that omega-6 greater than 11g/day (for adults) was required to overcome adverse health, and that the deficiency of omega-6

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[10] US Patent 7759507 (Jul 2010), teaching "omega-6 to omega-3 LCPUFAs of about 0.25:1 to about 3:1" (col 3).
[11] "*A New Way of Looking at Proteins, Fats and Carbohydrates*" http://web.archive.org/web/20070104020351/http:/whfoods.com/genpage.php?tname=faq&dbid=7#polyun mainstream public education website, The World's Healthiest Foods (WHFoods.com), run by The George Mateljan Foundation (non-profit) teaching, "ideal ratio of omega-3 to omega-6…is estimated to be around 1:2" (Annex AB).
[12] Bhagat U, "*Denying Patents on Applications of Discoveries Puts Public Health at Risk*" published online at https://www.ipwatchdog.com/2018/10/04/denying-patents-discoveries-puts-public-health-risk/id=101994 October 4, 2018 (Annex M)
[13] The'034 Application, Examples 11-27 (Annex A).
[14] *Ip et al.,* "*Requirement of Essential Fatty Acid for Mammary Tumorigenesis in the Rat*"; Cancer Research 45, 1997-2001, May 1985.
[15] Lands, Nutrition Reviews 1986:44-6:189-95; and Lands WE. "Dietary Fat and Health: The Evidence and the Politics of Prevention" Ann. N.Y. Acad. Sci. 1055: 179–192 (2005)

potentiates certain mechanisms, such that sudden increases in omega-6 have an overflow effect which can lead to myocardial infarction, strokes, infections, and physiological disturbances[16]. Later publications corroborated my findings.[17]

Thus, prior art was motivated to reduce subject's omega-6 intake because increases in omega-6 produced undesirable health effects. Skilled persons could not predict that higher levels of omega-6 fatty acids would produce desirable health effects, therefore, skilled person in prior art could not determine and practice the suitable dosages of omega-6 and omega-3 fatty acids for a subject taught in the subject applications.

I also found high amounts of omega-9 (monounsaturated fatty acids) to lead to adverse health, and phytochemicals and antioxidants to increase requirement for omega-6 and reduce requirements/tolerance for omega-3.

These discoveries were momentous because they set the stage for many more discoveries. Based on my discoveries I filed for patents in April 2008. The discoveries are explained in the above referenced applications (e.g., Annex A). The subject applications are intentionally written in layperson terms to raise awareness among the general public.

In his testimony of October 7, 2012 (Annex S), Dr. Erickson testified:
"The subject application contains very important focal points that were not understood prior to this disclosure. Most important of those as discussed above is that the prior art failed to fully understand the importance of omega-6 for health. Human and animal tissue contains many times omega-6 as compared to omega-3. Omega-3 can be preferentially metabolized. However, omega-6 has a shorter in-vivo life, possibly due to myriad of critical metabolites for which it is a precursor. Therefore, a lot more omega-6 is usually required as compared to omega-3. This disclosure indicates that deficiency of omega-6 is a greater problem. The disclosure focuses on the fact that certain nutrients including antioxidants and phytochemicals can effectively enhance omega-3 bioactivity in-vivo but inhibit the metabolism of omega-6. The risks of sudden increase of omega-6 or withdrawal of omega-3 have been explained, which was not previously appreciated or incorporated into dietary strategy. Prior dogma held that omega-6 causes disease, whereas this disclosure explains that the deficiency of omega-6 potentiates certain mechanisms, such that sudden increases in omega-6 have an overflow effect which can lead to myocardial infarction, strokes, infections, and physiological disturbances. Several examples have been given to manage menopause, sleep disorders, neural disease, mental function, musculoskeletal disorders, obesity, diabetes, digestive, reproductive, pulmonary, ophthalmologic, dermatologic, and immune functions. These are

[16] The'034 Application, Examples 11-27 (Annex A).
[17] Lu et al., Lipids in Health and Disease 2010:9:106.

multiple significant discoveries. Novel methods of treatment, administration, use, and tailored preparation are also disclosed. Because omega-6 and omega-3 significantly impact the structure and function of multiple physiological processes, correct delivery has a beneficial effect on many diseases. Sufficient directions are provided for the practitioner in the disclosure." Para [0023].

Subsequent to April 2008 priority date of the subject application the state of the art started to change. American Heart Association issued an advisory in 2009 to correct the perception that omega-6 are unhealthy[18]. In 2010, the US Department of Health and Human Services increased the recommended omega-6 intake in its Dietary Guidelines for Americans. Yet they did not teach all features in our applications and claims. Further, teaching is not sufficient as explained below.

2. Misconception That Teaching and Publication of Tables Listing Lipids in Foods Is Sufficient

Though the disclosure in our applications can be followed by general public, it is extremely difficult for public to obtain suitable dosages of lipids.

First, the public continues to be *misled* to believe that foods come with set nutrient (lipid) content as published in various tables listing nutrients in foods, such as olives and walnuts in Annexes B-E. In reality, nutrient content in foods varies based on genetics and epigenetics, and cultivating conditions, such as soil used, fertilizer used, hours of sunlight, and water composition, and from production batch to batch[19]. For example, olives have been found to have 3.5-21% omega-6 fatty acids content,[20] walnuts similarly vary in lipid content[21]. Therefore, all the published nutrient tables are giving us is nutrient content in the *tested batch* of the type of food, such as olives or walnuts.

Second, less than 1% of public can even name lipids—in a survey less than 1% of Americans correctly named six fats considered to be solid.[22] How can we expect them to consider minor lipids such as vitamins like A, E, D, K, sterols, and polyphenols present in foods that are potent in micrograms[23], particularly from oils because they are absorbed differently than whole foods?

Finally, it is too complex for the public to formulate lipid dosages for different family members on a daily basis.[24]

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[18] Harris *et al.*, *Circulation* 200, 119:902-907.
[19] Erickson testimony, January 31, 2014, para [003] (Annex T).
[20] The Olive Oil Source, https://www.oliveoilsource.com/page/chemical-characteristics#Fatty
[21] Tsao et al., "Fatty Acid Profiles, Tocopherol Contents, and Antioxidant Activities of Heartnut (Juglans ailanthifolia Var. cordiformis) and Persian Walnut (Juglans regia L.)" J. Agric. Food Chem. 2007, 55, 1164-1169.
[22] International Food Information Council Foundation, 2011 Food & Health Survey.
[23] Tsao et al., supra.
[24] Bhagat and Das (Annex Y).

3. Tailored Lipid Dosages are Difficult to Implement

Tailored lipid dosages are difficult to implement because of the points made above in Section III.2. For example, how to tailor lipid dosages despite unpredictability in food sources, how to control dosages of minor lipids such as vitamins like A, E, D, K, sterols, and polyphenols, how to create a spectrum of products keeping total lipid intake in check, giving consumers a regimen but with variations to maintain flexibility and gastronomic appeal, and how to make it work in daily life?

The complexity of the products necessitates a novel commercial structure under the direction of skilled persons.

4. *Tailored Lipid Dosages are Economically Infeasible Business Without Sufficient Patent Scope*

The complexities described in Sections III.2 and III.3 in formulating and implementing tailored lipids dosages make implementing these solutions economically infeasible without sufficient patent scope. The profit margins in food products are too thin to support recovery of investment in specialized products *necessitating* novel infrastructure and public teaching to *rise above the noise* created by 1000s of oils, oil mixtures, nut mixtures, and supplements on the market.

However, when the innovative tailored lipid dosages are given sufficient patent protection, the limited exclusivity allows marketing the products at higher margins, making it feasible to invest in the novel infrastructure and public teaching.

5. The Patent System Disfavors Proper Patent Grant to Nutritional Solutions

There is a most definite bias against nutrition in the patent system evidenced by the prosecution history of the '034 Application at USPTO, the appeal review at the Federal Circuit, and the refusal of the Supreme Court to accept the petitions for review despite clear violations of the law and abuse of discretion.

USPTO's unwillingness to grant proper patent protection to nutrition solutions is evidenced by the following in the subject applications:

1. Despite the fact that claims were drawn to linking features—dosages fatty acids for ingestion by a subject—numerous restrictions were placed on the claimed subject matter forcing divisional application filing.[25]
2. Alleged that claims are not patentable being drawn to recipes[26], though they are drawn to mixtures comprising determined dosages of lipids based upon subjects.

[25] USPA 12/426,034 Office action dated October 14, 2010, p. 2.
[26] Office Action of October 11, 2013, p. 15.

3. Arbitrarily selected *only* the narrowest embodiments of oil mixtures for patent grant[27]
4. Several limitations were excised or discounted from the claims in order to limit the allowable subject matter to certain oil mixtures.[28] (See Section IV).
5. Arbitrary §§ 101 and 102 rejections were forced and maintained despite strong rebuttals with arguments and evidence.[29] (See Section IV).

Additional pressure was placed upon the Applicant during interviews in form of the following statements from USPTO, in order to force narrow position:

- The subject claims are inherent in nutrition.
- Patents on omega-6 and omega-3 have to be restricted because many people work with them.

However, inherency can only be alleged if the prior art (nutrition) necessarily functions as claimed, which it does not. Rather the art overwhelmingly teaches the opposite, including in the cited references, as demonstrated above in Section III.1 and below in Section IV.1.

Further, restricting patents on omega-6 and omega-3 because many people work with them all but ensures that there will never be any meaningful advancement in this art. Many people work with restricted formulations is precisely why there is so much confusion and so much noise in the art. Everybody enters the market place and sells products based on the artificially patent-created boundaries, marketing to masses with conflicting marketing messages. This is how omega-3 got out of hand and hyped out of context in the first place, because many restricted patents on omega-3 have been issued.

The restrictions are in part because of USPTO's revenue maximization drive. Higher number filings, restricted patent grants, and divisional applications, all increase revenue to USPTO. Therefore, USPTO is happy to give composition A to Party-1, composition B to Party-2… and composition ZZZ to Party-nnn. These restrictions especially are applied to nutrition patents. This keeps revenue rolling in to USPTO and inventors given token patents and some revenue stream, but public confused, ill, and on drugs, because nobody truly gets the head or the tail and a system is set that perpetuates confusion.

Most important goal of USPTO is advancement for the betterment of human condition, revenue comes second. If USPTO inhibits advancement for revenue, then USPTO is failing its goal.

[27] USPA 12/426,034 Interview Summary mailed by USPTO on January 31, 2014, finding only narrow oil mixtures (3) and (4) in then claim 91 to be allowable.
[28] USPA 12/426,034 Office action dated March 10, 2015, p. 4-6.
[29] USPA 12/426,034 Office actions dated September 22, 2015 and PTAB Decision dated April 15, 2016 (Annex G).

This unfavorable treatment of nutrition patents is also evident from the Federal Circuit's review of the appeal in case of the '034 Application. For example, the Federal Circuit Opinion (Annex H) states at middle of page 5,

> The Board found that the "casing" and "dosage" terms do not impart patentability to the claimed compositions, and we agree, for the specification states that these claim elements are not limiting, and does not describe any assertedly novel characteristics of these components or their formulations.

The allegation that the limitations "casing" and "dosage" are "not limiting" is in violation of a large body of the Federal Circuit's own and Supreme Court's precedents and ruthlessly obliterates the Specification. For example, in *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979-81 (Fed. Cir. 1995) (en banc) the Federal Circuit stated,

> "Both this court and the Supreme Court have made clear that all elements of a patent claim are material, with no single part of a claim being more important or "essential" than another. See *Fay v. Cordesman*, 109 U.S. 408, 420-21, 3 S.Ct. 36, 243-45, 27 L.Ed. 979 (1883); *Pennwalt Corp. v. Durand-Wayland, Inc.,* 833 F.2d 931, 936 (Fed.Cir.1987) (in banc)."

Further, the Specification never said that "these claim elements are not limiting". The importance of "dosage of omega-6" is the most important feature in the Specification, emphasized throughout, especially in tables 10-14 and 21, Examples 11-27 and original claim 3. Specification paragraph [00106] specifically states, "It is intended that the following claims define the scope of the disclosure."

Then on what basis did the Federal Circuit decide that "casings providing controlled delivery of the formulation to a subject" and "dosage" recited in the claims is not limiting?

Additionally, the Federal Circuit itself has ruled in a large number of cases (see Section IV.1.iii-ix below) that the prior art must necessarily function as claimed and a competitor must be able to obtain the claimed subject matter from the prior art to be considered anticipatory.

Then on what basis did the Federal Circuit opine contrary to its own holdings?

Furthermore, in *Berkheimer v. HP, Inc.*, 881 F.3d 1360 on February 8, 2018, in case of a software patent (one month before issuing the problematic opinion in case of the '034 Application), the Federal Circuit held,

> "The question of whether a claim element or combination of elements is well understood, routine and conventional to a skilled artisan in the relevant field is a question of fact. Any fact, such as this one, that is

> pertinent to the invalidity conclusion must be proven by clear and convincing evidence. *See Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 95 (2011)…Whether a particular technology is well-understood, routine, and conventional goes beyond what was simply known in the prior art. The mere fact that something is disclosed in a piece of prior art, for example, does not mean it was well-understood, routine, and conventional."

Yet in case of '034 Application, which repeatedly asserts that the subject matter is poorly understood (e.g., see paragraphs [006]-[007], Annex A) and despite <u>eleven</u> testimonies from skilled persons to this effect (see subset in Annexes S-X) and numerous publications (Annexes Y-AB), and the cited art itself teaching the opposite, the Federal Circuit uttered <u>not even a single word</u> about this in its opinion (Annex H). In face of all the evidence, the Federal Circuit rather apathetically stated, "claims are directed to the omega-6 and omega-3 fatty acids that occur in nature" (Annex H, p. 12), disregarding the numeric limitations in the claims.

Further, *exactly one day* after the Federal Circuit affirmed *Berkheimer v. HP, Inc.*, refusing to rehear the case by a near-unanimous *en banc* decision (May 31, 2018), the Federal Circuit refused to reconsider its <u>*exact opposite ruling*</u> in the present case upon the Petition for Rehearing and Rehearing En Banc on June 1, 2018 (Annex I).

These violations of the USPTO and the Federal Circuit have been repeatedly called to the attention of the Supreme Court in several petitions (see Annexes K-Q). The Supreme Court has turned a deaf ear, thus far.

Thus, the entire US patent system disfavors patent grant to nutritional solutions, which the rest of the world follows, creating unfavorable economics for prevention and grave patent-practice-made humanitarian crises. See discussion below in Section V.

6. Special Interest Groups Including the Patent System Thwart Preventative Efforts

It is self-evident that the treatment industry, the sellers of drugs and devices and the providers of surgical and other procedures, work against preventative efforts such as tailored lipid dosages, but that the patent system run by the Government of the United States would thwart such efforts, as evidenced above and below is most disturbing. Significant patent scope is not only necessary to rise above the noise in the art, but also to fend off the efforts of those who undermine such efforts. Therefore, at least the Government should not compromise the effort by unnecessarily restricting the nutrition patents.

IV. Mutilation of Title 35 USC in Examination and Appeal Review of the '034 Application

1. USPTO Mutilated Title 35 of the United States Code and a Large Body of Case Law to Sustain Rejections

USPTO mutilated the law and wiped out the separation between 35 USC §§ 101, 102, and 103, usurping Congress' power and purpose behind those separations to an extreme that has never been done before.

In *six Office actions* over several years USPTO was unable to sustain § 102 rejections because no prior art taught identical claimed features, and § 103 rejections could not be sustained because of new insights presented, disadvantages predicted in the prior art, unexpected results, and opposite teachings in the prior art and critical unmet public health need. Thereafter, in the *7th Office action* in October 2013 and onwards USPTO mutilated the claims and the law and *forced* §§ 101 and 102 rejections.

As evidenced in Section III.1 above, prior to April 2008 the art overwhelmingly taught the opposite of the claimed inventions: low intake of omega-6 and low omega-6 to omega-3 ratios, and high intake of omega-9 (monounsaturated fatty acids), and failed to understand peculiar dose-effect of omega-6. A prior art teaching the claimed combinations has not surfaced in 10 years of worldwide prosecution of the corresponding applications. This bears out in *all* of the citations by USPTO.

For example:

- Cited arts under § 101: Olive Oil (Annex B) and Walnut Oil (Annex C) are interactive webpages describing nutrient content in a batch of each oil in capacity measures ranging from 1 tsp to 1 cup, and 4g to 100g. That is neither are the references teaching "dosage [amount determined for administration]" of omega-6 and omegae-3, nor are the references teaching "intermixtures of lipids" in "casings" to control lipid content/delivery or provide daily variety as taught in Specification (Annex A, e.g., paragraph [0030] and Table 3).

- Cited arts under § 102: Olives (Annex D) and Walnuts (Annex E) found on archives of whfoods.com webpages also describe nutrient content, specifically reciting "Nutritional Profile" on each of the main pages of Olives and Walnuts and "In depth nutrient analysis" on the associated pages. Furthermore, under "How to Enjoy" each of the Olives and Walnuts pages teach mixing olives/ walnuts with other foods and the website teaches "ratio of omega-3 to omega-6…around 1:2…decrease the

amount of omega-6 fatty acids in your diet, while increasing the amount of omega-3 fatty acids" (Annex AB).

- Cited art under § 102: Mark (Annex F) is inoperable and it teaches little of relevance to current claims because it teaches contradicting omega-6 to omega-3 ratios in col.2.ll.37-38 versus col.4.ll.21-25; it teaches incomplete lipid profile in the table in column 4 (86% of fatty acids in line 60); it gives an inoperable table in column 6 ("whey" is 100% yet other ingredients are present); it does not teach dosage of omega-6; and it does not teach the effect of other lipids on the requirements of omega-6. Skilled persons have testified to Mark's inoperability and their inability to arrive at the claimed inventions from Mark. See Annex T para [004], Annex U para [005] and [0022], Annex V para [0010] and [0013], Annex W para [009]-[0017], and Annex X para [3.3.10., and 3.4].

In order to support the rejections, USPTO gave no weight to the limitations "formulation", "dosage", and "casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids from different sources" and alleged that "intermixture of lipids from different sources" is a product-by-process limitation.[30] Similarly, many limitations were written out of the claims, for example, "daily amounts of fatty acids for the subject based on one or more factors selected from…" from Claim 98.

Further, even after *admitting* that the combination of ratios recited in Claim 102, 107, and 119 does not occur in nature, USPTO rejected the claims under § 101 for *combining* fatty acids that occur in nature into the formulation of the claims.[31]

Furthermore, not only did USPTO erroneously treat oils as "products of nature"[32] but they also improperly treated the man-made instructions on the webpages as "product of nature." All 55 claims were ruthlessly rejected as being drawn to "products of nature," and patent ineligible under § 101. (See claims at the end of Annex A and USPTO Decision at Annex G).

After excising limitations, USPTO alleged that Applicant had not demonstrated marked structural differences or transformation over Olive Oil or Walnut Oil, citing Funk Bros. Seed Co. v. Kalo Inoculant Co., Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127 (1948) and *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.* 133 S. Ct. 2107 (2013).[33]

[30] PTAB Decision dated April 15, 2016, pp. 7—9 (Annex G).
[31] Final Office action dated September 22, 2015, p. 36.
[32] Oils are not products of nature; they are made from nuts/seeds and have different properties and nutrient content from nuts/seeds. Extensive arguments and evidence to this effect are on record.
[33] PTAB Decision dated April 15, 2016 pp. 9-14 (Annex G).

Both the citations of Funk Bros. and Myriad under § 101 were contrary to 35 USC § 101 and Congress' intent!

Funk Bros. was decided under the now obsolete 35 USC § 31 (1946) that governed *both* patent-eligibility and novelty, which described "Inventions Patentable" as:

> "Any person who has invented or discovered any new and useful art, machine, manufacture, or composition of matter, or any new and useful improvements thereof…not known or used by others in this country, before his invention or discovery thereof, and not patented or described in any printed publication in this or any foreign country, before his invention or discovery thereof..."

Congress using *its authority* had revamped Title 35 USC via the 1952 Patent Act, setting up *separate* standards for eligibility under § 101 and for novelty under § 102, and introducing *new standards for non-obviousness under § 103*. The 1952 act was enacted precisely because having eligibility and novelty decided together under one section was problematic, and because there was great ambiguity in what it means to "invent." Congress after great deliberations decided that among conditions for patentability *non-obviousness* was the correct statutory standard rather than "invention" because "invention" is meaningless and lacks clarity[34] and accordingly set the standards in § 103.

Congress set the test for patent eligibility under Title 35 USC §101 of the 1952 Patent Act as:

> "*Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title*."

Noticeably missing from §101 are the word "structural difference" or "transformation" as a precondition to "obtain a patent therefor", as required by USPTO. Also, what standard of "structural difference" or "transformation" is sufficient for patent-eligibility. As with "invention," there is no standard of "structural difference" or "transformation."

Thus, USPTO improperly applied *Funk Bros.* where alleged want of "invention" was the issue, which was overruled by Congress via the 1952 Patent Act. Further, USPTO improperly applied *Myriad*, where the claims were drawn to isolated DNA

[34] "*Efforts to Establish a Statutory Standard of Invention: Study of the Subcommittee of Patents, Trademarks, and Copyrights of the Committee on the Judiciary*" United States Senate; Eighty-fifth Congress, First Session Pursuant to Senate Resolution 55, Study No. 7 (published 1958)

and not expressed in terms of chemical composition. Even then the Supreme Court did find man-made cDNA to be patent-ineligible in *Myriad*.

In contrast, the subject claims are most clearly drawn to man-made *composites* of omega-6, omega-3, and/or other lipids "from different sources," and thus without a doubt the claimed *formulations* clearly fall within the ordinary, contemporary and common meaning of a "composition of matter" under § 101.

Further, the "casing" limitation also falls within the definition of a "manufacture" according to the common meaning of "manufacture" as in § 101.

Still further, the claims represent an important new and useful discovery in nutrition, and the USPTO de facto removed the word "discovers" from § 101.

USPTO usurped Congress' power and rewrote 35 USC § 101 as follows:

> "*Whoever invents ~~or discovers~~ any new and useful ~~process~~ transformation, machine, ~~manufacture, or composition of matter,~~ or any new and useful improvement thereof, may obtain a patent therefor...*"

This re-write of § 101 is an instance of extraordinary usurpation of judicial powers from interpreting statutes to completely redrafting them. It is most disturbing that the USPTO unlawfully abrogated the "discovery," "process," "composition of matter," and "manufacture" language actually found in 35 U.S.C. § 101 from numerous claims at issue in favor of vague concepts "structurally different" or "transformation" or "invention" that the Congress has expressly rejected in deliberations for the 1952 Patent Act.

USPTO also usurped Congress' power and rewrote 35 USC § 102. The rejections under § 102 are contrary to 35 USC § 102 and Congress' intent!

The legal requirements for anticipation rejection under § 102 are very *strict* and rightly so. In order to anticipate the applicable prior art must *disclose and enable the exact same invention* with every single element as recited in the claims. The underlying principle of anticipation rejection is that public—skilled persons including competitors—has been fully informed of the exact solutions and how to practice them and there can be no doubt about this. This is built into Title 35 USC.

> § 102 states,
> "*Novelty; Prior Art.—A person shall be entitled to a patent* ***unless****—*
> *(1) the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention...*" [Emphasis added].

In contrast § 103 states,
"*A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not* ***identically disclosed as set forth in section 102****, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains.*" [Emphasis added].

Specificity in patent law has always been held as not anticipated by general prior art disclosure, and *neither the USPTO nor the courts* have had any difficulty in examining and upholding *specific disclosure and enablement* as not anticipated by general prior art. See representative jurisprudence below:

i. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

ii. A reference disclosing "alkaline chlorine or bromine solution" embraces a large number of species and cannot be said to anticipate claims to "alkali metal hypochlorite." *In re Meyer,* 599 F.2d 1026, 202 USPQ 175 (CCPA 1979).

iii. Anticipation law does not permit to fill in missing limitations simply because a skilled artisan would immediately envision them. *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 851 F.3d 1270, 1274 (Fed. Cir. 2017).

iv. "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." In re Oelrich, 666 F.2d 578, 581 (CCPA 1981.

v. The anticipation analysis asks solely whether the prior art reference *discloses and enables* the claimed invention." "Under the principles of inherency, if the prior art *necessarily* functions in accordance with, or includes, the claim limitations, it anticipates." *Perricone v. Medicis Pharm. Corp*. 432 F.3d 1368, 1376 (Fed. Cir. 2005). [Emphasis added].

vi. The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art).

vii. In order to anticipate the claims, the claimed subject matter must be disclosed in the reference with "sufficient specificity to constitute an anticipation under the statute." What constitutes a "sufficient specificity" is fact dependent. If the claims are directed to a narrow range, and the reference teaches a broader range, other facts of the case, must be considered when determining whether the narrow range is disclosed with "sufficient specificity" to constitute an anticipation of the claims. Compare *ClearValue Inc. v. Pearl River Polymers Inc.,* 668 F.3d 1340, 101 USPQ2d 1773 (Fed. Cir. 2012) with *Atofina v. Great Lakes Chem. Corp,* 441 F.3d 991, 999, 78 USPQ2d 1417, 1423 (Fed. Cir. 2006).

viii. If little is known in the prior art about the nature of the invention and the art is unpredictable, the disclosure would need more detail as to how to make and use the invention in order to be enabling. *Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) ("the public's end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology.")

ix. "[A]nticipation under § 102 can be found only when the reference discloses exactly what is claimed and that where there are differences between the reference disclosure and the claim, the rejection must be based on § 103 which takes differences into account." *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985).

Thus, there is clear and *purposeful* distinction between lack of novelty and obviousness, in that the law recognizes that in order to destroy novelty a prior art document must disclose and teach how to practice the *identical* invention then only it can be said that this is in possession of the public. Furthermore, a selected range from a broader numerical range is considered novel.

For instance, if there were a reference that exactly described and enabled a formulation to cure common cold permanently, then common cold would be cured. It would defy every conceivable logic if there is a reference that exactly describes and enables the formulation to cure common cold (e.g., dosage of compound A above X g/day), yet billions of humans repeatedly suffer the misery of common cold. Therefore, it is flawless if a reference *exactly* describes and enables claimed limitations, then such claims are not novel.

However, if exact same formulation is *not* described in the prior art, it is *not* clear what aspect of the prior formulation is problematic (e.g., how much compound A in absolute and relative to compound B), and there are *opposite teachings* to the claimed formulation (e.g., dosage of compound A below X g/day) and the public continues to suffer from the misery (like common cold), then the claimed formulation (ratio of compound A to compound B Y:1 and compound A above X g/day) can neither lack novelty nor be obvious.

Thus, § 102 requires *identical* disclosure of the claimed subject matter, which requirement is not met by Olives, Walnuts, or Mark.

USPTO excised the specific differentiating features "dosages", "casings providing controlled delivery" and "intermixtures of lipids from different sources," in order to force rejections under § 102 because claims were non-obvious under § 103 because of new insights presented, disadvantages predicted in the prior art, unexpected results, and opposite teachings in the prior art and critical unmet public health need.

Furthermore, USPTO reconstructed Mark that gives *no* teaching about "dosage of omega-6 fatty acids" *no* teaching of how other lipids affect the activity of omega-6 under § 102. Because Mark recited contradicting omega-6 to omega-3 ratios in col.2.ll.37-38 versus col.4.ll.21-25, and gave inoperable tables in columns 4 and 6, USPTO reconstructed Mark's recitation "the source of omega-6 fatty acids is present in the range of approximately 4-6% of the total calories. The omega-3 fatty acid source preferably present in the range of approximately 0.8-1.2% of calories"[35] into ratio of omega-6 to omega-3, though same source can be source of omega-6 and omega-3 (e.g., canola oil) rendering the recitation meaningless; and USPTO reconstructed concentration (g/1000 ml) into dosage. Mark also does not *necessarily* function as an "intermixture of lipids from different sources," reciting "a lipid source" in claim 1, 9, and 15. (See Annex F). Thus, USPTO cherry-picked Mark recitations and combined as convenient to sustain rejections.

Olives, Walnuts, and Mark rejections, which would have been applied under § 103 were applied under § 102 because § 103 could not be sustained due to opposite teachings in the art—including in Olives, Walnuts, and Mark.

In any case, Mark is not dispositive because subject Claim 91 and dependent claims, and subject Claim 82, which can replace independent Claim 65, are not rejected under Mark.

Thus, this is an *extreme case of improper rejections by USPTO* of an extremely important invention directed to "composition of matter" "dosages" and "controlled delivery" over *individual foods* under §§ 101 and 102 despite opposite teachings in the art as a whole including the cited art. Though tables describing possible content of *some* nutrients in *individual foods* are in public domain, but popular media, international scientists, various governments, and industry overwhelmingly teach to mix these foods to achieve low absolute and relative intake of omega-6 fatty acids[36]? *In other words, the individual foods in the prior art have neither disclosed nor enabled the solutions nor solved the public suffering.*

[35] PTAB Decision dated April 15, 2016, pp. 19-20 (Annex G).
[36] Ip et al. 1985 supra; Lands 1986 supra; Simopoulos et al. 1999 supra (Annex Z); Lands 2005 supra (Annex AA); WHFoods.com (Annex AB); Wikipedia (Annex AC).

Neither would an individual food composition enable a skilled person to inevitably practice omega-6 dosages as taught in the subject disclosure based on state of the art at the time of the disclosure, nor would it be immediately apparent to skilled person to practice the dosages as taught and consider omega-6 concentration in relation to total lipids from individual foods, nor is it proper to interpret equivalents not disclosed in the references, that is a matter of obviousness. Furthermore, as evident from Annex AC, there is still debate in the art on the claimed subject matter. Therefore, at least lack of enablement in the cited art is a dispositive point to ruling non-anticipation.

Holding scope of the inventions against the Applicant USPTO rejected *all* claims under the pretext of §§ 101 and 102 because rejections under § 103 could not be sustained, and USPTO wiped out the separation between §§ 101, 102, and 103 and usurped Congress' power and purpose behind the separations.

2. US Court of Appeals for the Federal Circuit Rubberstamped USPTO Without Meaningful Review as Required by Administrative Procedure Act

The Federal Circuit affirmed the USPTO in March 2016, without giving a meaningful review, and issued an evasive disjointed opinion. See Annex H.

The case demonstrates *astounding breadth* of abuse of discretion by the Federal Circuit *at least on the following eight counts*:

i. Condoned USPTO's mutilation of the claims by excising limitations,
ii. Condoned USPTO's rewriting of §101 to strike, "composition of matter", "manufacture", and "process" from the statute,
iii. Condoned USPTO's requirement of "structurally different" or "transformation" under §101,
iv. Failed to cite eligibility and anticipation law based upon which the case is decided,
v. Failed to meaningfully review §102 rejections,
vi. Acknowledged prosecution disclaimer of single source like olives/walnuts, then disregarded it and affirmed §102 rejection over olives/walnuts anyway,
vii. Failed to review many claims including independent claims 91,
viii. Dismissed *eleven* expert testimonies, without a word in the opinion.

The opinion jumps from one context to another inexplicably; one doesn't know which claim is being reviewed and what law is being applied. For example, at page 10 opinion states,

> "The Applicant also argues that claim 128 is distinguished from natural products, and is not anticipated based on the limitation

> that the compositions contain "nuts or their oils" obtained from "almonds, peanuts, and/or coconut meat." The Board held that admixture with other natural products of known composition was not shown or stated to change the nature of the compositions, citing *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 131 (1948)…The Board correctly held that claim 128 does not avoid the rejection on the ground that the claims are directed to known natural products."

However, Claim 128 is dependent on Claim 91, which the Federal Circuit *never reviewed*. How can Federal Circuit opine upon a dependent claim without reviewing the elements of the independent claim first? Further, Funk Bros. citation against Claim 128 is the only citation under § 101 by Federal Circuit, there is no other citation even under §102. So one is left guessing as to what principles of law are being applied?

Further, at page 11 the opinion states,

> Claim 102 recites specific ratios of **polyunsaturated, monounsaturated**, and saturated fatty acids. Claims 107 and 119 present the fatty acid content recited in claims 98 and 91, respectively, in Tables in the specification. The Board observed that the servings of olive oil and walnut oil shown in the references contain **omega-6 and omega-3 fatty acids in amounts within the Applicant's claimed ranges**. Thus the Board held that the "intermixture of lipids from different sources" does not distinguish the claims from natural products because the Applicant "has not provided adequate evidence that an oil from different sources would necessarily have a composition that is different from one from the same source, nor that a different source would necessarily impart characteristics to the formulation which were absent when a single source was used." Board Op. at *8. [Emphasis added].

However, the Federal Circuit comments above pertain to Claim 65 not claims 102, 107, and 119. For example, what do "omega-6 and omega-3 fatty acids in amounts within the Applicant's claimed ranges" have to do with "ratio of monounsaturated fatty acids to polyunsaturated fatty acids?" The Federal Circuit *failed to answer* the argument that claims 102, 107, and 119 expressly recite numeric limitations directed "***ratio of monounsaturated fatty acids to polyunsaturated fatty acids* is in the range of 1:1 to 3:1**"[37], which is *not* met by olive oil or walnut oil.

[37] Appeal Brief p. 34, 58-59, 77-78.

It is well established that failure to answer an argument is tantamount to conceding that there is no answer. The opinion was intentionally written evasively and in a disjointed manner to evade justice, because the Federal Circuit had no answer. There is not one instance of impropriety but improprieties on all counts. The Federal Circuit's improprieties were also established above in Section III.5.

The whole point of the claimed inventions is that nature does not provide the required nutrients in desired combinations and restrictions and is unpredictable. The allegation that the claimed products occur in nature is an oxymoron. The Federal Circuit's actions demonstrate the system's bias against nutrition.

One does not expect such travesty of justice from the Federal Circuit, the second highest court in the nation. This is extremely demoralizing for the citizens, above and beyond the public health consequences.

3. Reticence of the Supreme Court of the United States

The Supreme Court has not accepted the Petition for a Writ of Certiorari (Annexes K-M) (case no. 18-277) and the Supreme Court has overlooked the extreme abuse of discretion in examination and appeal review and denied the Petition for a Writ of Mandamus (Annexes N-P) (case no. 18-1274).

In view of intervening circumstances in the form of the US Senate's recently published proposed language to reform Title 35 U.S.C. § 101 based on problematic behavior of the USPTO and the lower courts[38], Petition for Rehearing for the Writ of Certiorari (case no. 18-277) was submitted to the Supreme Court on July 11, 2019 (Annex Q), which is currently pending.

It is disturbing that the Supreme Court considers it more important to protect the constitutional rights of heinous criminals, see *Kennedy v. Louisiana*, 554 U.S. 407 (2008) under the 8th Amendment to not be subjected to "cruel and unusual punishment" than protecting the same rights of general public to not be put under the knife or subjected to drugs and devices unnecessarily, which happens when patent system favors patent grants to drugs over nutrition.

Additionally, the Supreme Court disregards constitutional rights of inventors to due process and equal protection of laws under the 14th Amendment. Supreme Court should have afforded the same protection of laws to the Applicant and Inventors, such as to *Dickenson v. Zurko*, 527 U. S. 150 (1999) holding "the importance of not simply rubber-stamping agency fact-finding." Id 162., and to *Myriad* finding cDNA to be patent eligible.

The Supreme Court's declinations are further travesty of justice.

[38] https://www.tillis.senate.gov/services/files/E8ED2188-DC15-4876-8F51-A03CF4A63E26

V. Patent Practice-made Humanitarian Crises

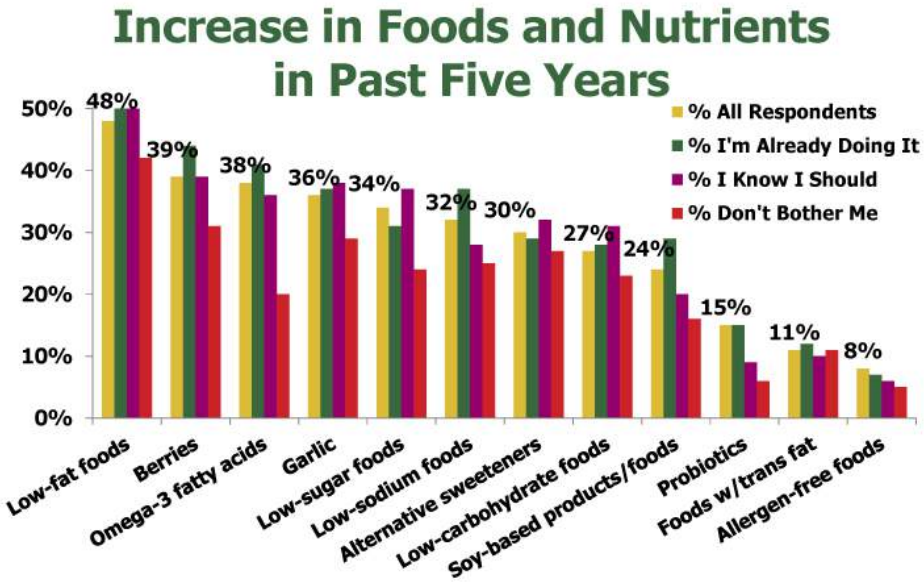
The dubious patent practices discussed above have created at least two kinds of humanitarian crises, first towards the public at large, and second towards independent inventors and small entities.

1. Humanitarian Rights Violations of Public at large

Though Title 35 USC does not differentiate patent grant to nutrition versus drugs, but as evidenced above patent practice does. If Applicant's claims were directed to a drug candidate similarly differentiated over the prior art, the patent would have been granted many years ago.

When patents are favourably granted to drugs and devices it makes them more financially rewarding, enabled by the large profit margins from prompt and strong monopoly. Then, investors, marketers, and providers heavily fund and tout drugs and devices and make public dependent on drugs and devices.

When nutrition patents are granted, they are severely restricted which causes confusion and makes the problem worse, as USPTO has done in the subject case under the pretext of §§ 101 and 102. Piecemeal patents do not solve problems and cannot advance nutritional arts. Rather, they create more confusion and excesses/ imbalances of certain foods and nutrients in the nutrition supply and individual consumption, as evidenced by Nutrition and You: Trends 2008; Survey by American Dietetic Association.[39]



[39] http://www.eatrightpro.org/~/media/eatrightpro%20files/media/trends%20and%20reviews/nutrition%20and%20you/trends_2008_presentation.ashx; slide 37.

For example, Applicant pointed out in examination of USPA 13/877,847 that Examiner is improperly restricting the claims to small amount in the package, rather than dosage customarily indicated on product packaging, allowing multi-dose packaging, and that the restrictions will force the pricing of the claimed consumer product out of the market and multiply packaging and create waste and burden the environment and humanity. Examiner responded that it was not her problem and forced the restriction under the pretext of clarity.[40]

Thus, thousands of patents are granted on very restricted formulations and methods leading to advertising campaigns that cancel each other out and cause mass misinformation. This leads to total confusion and public stops believing everything.

Therefore, the patent system is obstructing advancement in nutrition.

The misdirected patent policy is why public has been paying for lipid patents since 1870s[41] but the problem has not gone away. The very issue is that patent protection is not provided to formulated lipid dosages for subjects, which is the necessary foundation, but patent protection is provided to a restricted amount in a package, or different oil mixtures, or structurally altered molecules, or designing new oil varieties, which is of limited value because lipid content will still depend on where and how a species is cultivated.

Such missteps take us farther and farther from genuine solutions, in the meantime more harm is caused to public health. For example, it was a German patent of structurally altered fats[42] that gave us hydrogenated fats and caused worldwide diseases for 100 years[43], which activity is still ongoing[44] despite damage caused previously.

Thus, occasionally, some oils, mixtures, molecules are promoted but then they realize it does not solve the problem or causes more problems and come back to square one. The result is lipid delivery to public has not substantially advanced in 6000 years, since invention of oils. Though oil manufacturing has advanced, but to date random oils are randomly added to foods.

Thus, the patent practice is skewing the marketplace in favor of drugs and devices and taking public farther from prevention, while the public continues to suffer. As noted above 117 million Americans from suffer from chronic diseases and 80% of women suffer from hormonal issues, which can be abated by tailored lipids.

This is a humanitarian crisis from which public has been suffering for at least 100 years, since industrialization of nutrition started to prevail. If patents were equitably granted to nutrition and drugs, then at least nutrition and prevention

[40] USPA 13/877,847 Office action dated August 13, 2018, p. 20-21.
[41] https://en.wikipedia.org/wiki/Margarine
[42] https://en.wikipedia.org/wiki/Wilhelm_Normann
[43] https://en.wikipedia.org/wiki/Crisco
[44] E.g., U.S. Patent 9,351,502 "Oxidized and partially hydrogenated oil or fat" issued May 31, 2016

have a fair chance. However, in the current scenario, where the patent system has compromised and sabotaged efforts such as ours with undue restrictions and 10 years of delay in patent grant, nutrition has little chance and the crisis may get more severe.

Net effect is that the patent system is not only obstructing advancement in nutrition, but it is promoting stagnation in nutrition. By obstructing advancement in nutrition, the system is obstructing advancement in medicine also, because we as a society are so consumed in treating what can be prevented that we are not making true downstream advancements in medicine that address issues beyond what can be prevented.

2. Humanitarian Violations of Independent Inventors and Small Entities and Worldwide Consequences of Actions of the USPTO and the Federal Circuit

The patent system neutered our innovation with obstruction and delays because of its bias against nutrition and because they are programmed to restrict. Although, USPA 13/332,251 was granted in May 2019 (US Patent 10292958), it is 10 years after the parent application was filed and after numerous Office actions and appeals and enormous prosecution costs and business setbacks to the Applicant.

It is extremely arduous for small entities and independent inventors to sustain such long prosecution (10 years in the present case). We have had lawyers prosecuting for us off and on, but as a small company we cannot keep that up for 10 years. As a result, we had to self-prosecute before the Appeal Board at USPTO and the Federal Circuit, which apparently was held against us as evident from the impropriety of the decisions discussed above. In other words, first they compromise small companies with improper objections and delays, and then when small companies are forced to self-prosecute, they hold self-prosecution against the applicants.

This case also illustrates that *pro se* inventors cannot get fair treatment at USPTO or the Courts. As evidenced above in Section III.5, the Federal Circuit gave a favorable treatment to Berkheimer and exactly opposite to us even though the issue of poorly understood factors is stronger in our case than the Berkheimer case. Further, why is the Berkheimer case getting Supreme Court's attention[45] and not ours, though our case has 1000 times more national significance? Only because HP Inc., a big business, filed the petition.

Furthermore, in this case there is evidence of EPO (European Patent Office) copying USPTO's improprieties[46], and many other jurisdictions in turn have copied

[45] https://www.supremecourt.gov/search.aspx?filename=/docket/docketfiles/html/public/18-415.html
[46] Alleged anticipation by individual oils was brought up for the first time by EPO at the Oral Proceedings held on 11 February 2015, following USPTO's allegation of anticipation by individual oils as alleged "products of nature" in the

EPO's and USPTO's improper actions. That is *the Governments are violating independent inventors/small entities (and the public) in collusion with each other*. Because of this collusion Applicant has had to file scores of extra responses to repeated improper objections and over dozen appeals and lawsuits in various jurisdictions.

Thankfully, some governing bodies in some other jurisdictions have demonstrated greater sense of responsibility, duty, and justice than the United States of America and EPO[47] thus far. For example, Intellectual Property High Court of Japan (in case of Japanese Patent application 2014-099072) and Intellectual Property Trial and Appeal Board of South Korea (in case of Korean Patent Application 10-2010-7026029) have reversed the decisions of their respective patent offices. South Korea has issued a Notice of Allowance, which patent covers claims similar to *both* the '034 Application and the recently granted US Patent 10292958.

However, imagine the burden all these actions have placed on the small company and its proprietors, and how this has obstructed innovation and reduced the time window to implement the critical innovation.

The prosecution delays impede implementation of innovation because investors and strategic partners do not come forward until patent scope is clear. By the time the patent is granted so little patent term is left that the necessary window to nurture the innovation in protected environment is gone.

It should be noted that disclosure or teaching is not always enough to solve a problem. In cases such the present one, the complex innovation will not take hold in the absence of a sufficient scope and protected term. Just like a tree sapling needs a fence around it to protect from cattle to allow growth, similarly such inventions need the twenty-year patent term for proper implementation. Therefore, the view that the patent system's objective is to induce disclosure, would be misplaced.

Such US practices (in collusion with other jurisdictions) have put human rights and sustainable development in jeopardy.

Office action of 18 August 2014 p. 14-20, in case of corresponding US patent application number 12/426,034. Additionally, EPO had raised some far-fetched objections copying the USPTO Examiner, such as referring to "different sources" as "different producer" or "different supplier." See Annex AD.

[47] The injustice at EPO has been called to the attention of the Administrative Council of EPO. See Annex AD.

VI. Conclusion and Remedy Requested

Since USPTO rejection in 2015 in the '034 application, over four years have been lost in appeals at the expense of innovation and public health. USPTO and the Courts successfully obstructed the innovation and public well-being and failed to render justice.

They defeated the very purpose of patents, innovation for betterment of the human condition, the very reason for USPTO's and the patent system's existence!

The Federal Circuit should have shown grave concern upon such violations happening at USPTO that are abusive to inventors, applicants, and are sabotaging implementation of innovation for public benefit. Under the circumstances the Federal Circuit should have reversed the USPTO.

These actions are extremely detrimental to innovation, public benefit, and the USPTO's charter.

We request the Congress to take action to stop this malfeasance and request the following remedies:

1. Abrogate the USPTO's and the Federal Circuit's Decisions in case of the '034 Application.
2. Due to the extraordinary case of malfeasance on part of the USPTO and the Federal Circuit, adjust the patent term such that the 20 years patent term is counted from the date of allowance of the '034 Application. In the worst case, no more than three years may be deducted from the 20-year patent term for prosecution as per 35 U.S.C. § 154.
3. Reconsider revenue and reward at USPTO, removing incentives for unnecessary restrictions that compromise innovation, and place burden on humanity.

Unless the Congress fully supports this endeavor the current stagnation in the lipid nutrition and the associated public suffering will likely continue for 1000s of years to come.

Respectfully,

Urvashi Bhagat

Urvashi Bhagat
Chief Executive Officer

ANNEX A:

US Patent Application 12/426,034 filed on April 17, 2009

LIPID-CONTAINING COMPOSITIONS AND METHODS OF USE THEREOF

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application claims priority to U.S. Patent Application Ser. No. 61/046,747 filed on April 21, 2008, U.S. Patent Application Ser. No. 61/075,708 filed on June 25, 2008, and U.S. Patent Application Ser. No. 61/111,593 filed on November 5, 2008, all of which are incorporated by reference herein in its entirety for all purposes.

BACKGROUND

[0002] Fatty acids play important physiological functions. They are the building blocks of phospholipids and glycolipids, crucial components of cell membranes. Fatty acids are the best biological fuel molecules, capable of yielding more than twice as much energy per gram as produced by carbohydrate or protein. Fatty acids directly affect the functions of many proteins through covalent modifications of such proteins. Fatty acids affect membrane fluidity and associated cellular processes. Fatty acids are also involved in gene regulation, as such may be used to optimize expression of certain genes. Fatty acids' derivatives are also important hormones and biological messengers, e.g., prostaglandins, thromboxanes, leukotrienes, lipoxins, and resolvins. These hormones and messengers affect a broad range of physiological functions such as vasal dilation, platelets aggregation, pain modulation, inflammation, and cell growth.

[0003] The human and animal bodies synthesize many kinds of fatty acids of various length of the carbon chain, with various numbers and locations of double bonds. The addition of double bonds into a fatty acid chain converts it into an unsaturated fatty acid, which play significant roles in physiological functions. One way of tracking the location of the double bond in an unsaturated fatty acid molecule is by its distance from the distal carbon, i.e., the omega-carbon. For example, the 18-carbon oleic acid, which has a double bond at the 9^{th} carbon from the omega position, is called omega-9 fatty acid. Table 1 below describes various unsaturated fatty acid groups named according to their double bond locations relative to the omega position:

Table 1. General Descriptions of Some Fatty Acids

Name of Fatty Acid	General Formula	Starting Molecule for Biosynthesis
Omega-3	CH_3-CH_2-CH=CH-R-COOH	Alpha-Linolenic Acid
Omega-6	CH_3-$(CH_2)_4$-CH=CH-R-COOH	Linoleic Acid
Omega-7	CH_3-$(CH_2)_5$-CH=CH-R-COOH	Palmitoleic Acid
Omega-9	CH_3-$(CH_2)_7$-CH=CH-R-COOH	Oleic Acid

[0004] As shown in the table above, Linoleic acid (LA) and Alpha-linolenic Acid (ALA) are the precursors for all omega-6 and omega-3 fatty acids. It is well established that LA and ALA are "essential" fatty acids. They must be supplied in the diet because the human and other mammalians cannot synthesize them from other sources. Dietary deficiency or excess of the two essential fatty acids may cause many illnesses. It is also well known that LA and ALA share the same metabolic pathways, and that the excess of one can increase the need for, or create a deficiency of, the other. Along with LA and ALA, certain other fatty acids, such as Oleic acid and certain saturated fatty acids are also considered important for human nutrition even though the body can make them. The latest science also shows evidence that non-essential fatty acids though beneficial in optimal quantities, can interfere with the activity and metabolism of essential fatty acids when in excess, and that the quantity of dietary fat can also influence the metabolism of fatty acids. ALA is known to be preferentially metabolized by the human body depending on the amount of the other fatty acids present in the diet.

[0005] Evidence also shows that antioxidants, phytochemicals, microorganisms, vitamins and minerals, other dietary factors including proteins and carbohydrates, and hormones and genes also play a role in metabolism of essential fatty acids. Furthermore, human studies have identified that males and females appear to differ in their ability to metabolize essential fatty acids. It has been suggested that sex hormones play a role in these differences. Molecules of polyunsaturated fatty acids have a zigzag-like structure because of the double bonds. Because they are flexible and do not pack tightly, they stay fluid even at cold temperatures and collectively lend flexibility to tissues. Hence, in colder climates the human body benefits from greater amounts of polyunsaturated fatty acids. However, greater

the number of double bonds in a lipid molecule, greater the susceptibility to per-oxidation, which may be associated with a number of diseases and may accelerate aging. This is another reason for cautious consumption of polyunsaturated fatty acids.

[0006] Numerous studies provide evidence for the prophylaxis and treatment of medical conditions using supplementation with omega-3 fatty acids and recommendations to reduce omega-6 fatty acids consumption. The medical conditions implicated include menopause, cardiovascular diseases, mental disorders, neural disorders, musculoskeletal disorders, endocrine disorders, cancer, digestive system disorders, symptoms of aging, viral infections, bacterial infections, obesity, overweight, renal diseases, pulmonary disorders, ophthalmologic disorders, dermatological disorders, sleep disorders, dental diseases, and the diseases of the immune system including autoimmunity. For example, U.S. Patent No. 5,780,451 taught lipid formulations for patients with ulcerative colitis, which include omega-3, omega-6, and omega-9 fatty acids. The omega-3 fatty acids content in these lipid formulations was significantly high. Similarly, a recently published U.S. patent application, US2008/0039525, disclosed lipid compositions used for diabetic patients, which contained omega-3, omega-6, and omega-9 fatty acids, with the specific ratio of omega-6 to omega-3 being between 0.25:1 to 3:1.

[0007] The traditional emphasis on increasing omega-3 fatty acids and reducing omega-6 fatty acids consumption often does not result in satisfactory relieves because of the uncertainties introduced by dietary and demographic factors. Accordingly, improved methods and treatments, using improved lipid compositions, for the medical conditions and for prophylaxis are still needed. In fact, on January 26, 2009, for the first time the American Heart Association issued an advisory to correct the perception that omega-6 fatty acids are unhealthy (http://americanheart.mediaroom.com/index.php?s=43&item=650). The current methodologies are confusing for the consumers, hence lead to over consumption or under consumption of critical nutrients with major health consequences.

BRIEF SUMMARY

[0008] The present disclosure relates to compositions and methods for prophylaxis and/or treatment of medical conditions linked with an imbalance in one or more lipids within context of other factors. More particularly, the present disclosure relates to

the use of compositions and methods that use more advantageous sources of omega-6 fatty acids, in the presence of nutritionally adequate omega-3 fatty acids. The disclosure also relates to methods and compositions that deliver omega-6 and omega-3 fatty acids along with other nutrients that optimize the daily delivery and bioavailability of omega-6 and omega-3 for prophylaxis and/or treatment of medical conditions linked with an imbalance in one or more lipids. This disclosure also relates to methods of steady delivery of the bioactive substances, daily, weekly, monthly or longer duration wide and sudden fluctuations of which may be harmful. Furthermore, this disclosure also relates to methods of daily delivery of essential fatty acids within the optimal range with respect to the recommendations.

[0009] One general embodiment of the present disclosure is a lipid-containing composition comprising optimal amounts of fatty acids, antioxidants, minerals, and phytochemicals/ plant matter for a mammalian subject based on one or more factors selected from the group including the subject's age, sex, diet, bodyweight, physical activity, medical conditions, and the climate of the subject's living area. Such composition is administered to a subject through a steady delivery process, as explained later, according to one embodiment of the disclosure. According to another embodiment of the disclosure, the fatty acid, antioxidant, mineral, and phytochemical components of the composition's lipid contents are achieved at least in part by using one or more of the following concentrated lipid sources: oils, butters, nuts, and seeds.

[0010] Another embodiment of the disclosure is a lipid-containing composition comprising polyunsaturated, monounsaturated, and saturated fatty acids, wherein the ratios and amounts of said three fatty acid types are controlled based on one or more of the following factors for a mammalian subject: age, sex, climate, body weight, physical activity, diet, and medical conditions.

[0011] Another aspect of the present disclosure is a specific lipid composition suitable for administration to a mammalian subject. One embodiment of such composition comprises three or more of the following substances (or the oil thereof) in certain defined concentrations: peanuts, almonds, olives, soybeans, cashews, flaxseeds, pistachios, pumpkin seeds, sunflower seeds, sesame seeds, walnuts, anhydrous butter oil, and coconut meat. Another example of such composition comprises

three or more of a safflower oil, sunflower oil, peanut oil, almond oil, corn oil, and anhydrous butter oil.

[0012] Another aspect of the present disclosure is directed at methods of prophylaxis or treatment of a medical condition for a mammalian subject, said method comprising administering a therapeutically effective amount of balanced lipid formula to said subject, preferably replacing the unbalanced fats typically added to foods in form of oils, butters, nuts and seeds and the like.

[0013] Yet another aspect of the present disclosure is directed at methods of creating lipid and other nutrients-balanced diet by combining special formulated lipid composition with lipid-free or low-lipid food.

DETAILED DESCRIPTION

[0014] As used herein, "prophylaxis" refers to the preservation of health, a preventive treatment, or a treatment meant to reduce the risk of a medical condition.

[0015] As used herein, the term "treatment" in the context of a medical condition refers to the management of the condition and may or may not involve the complete amelioration of the condition.

[0016] As used herein, "medical condition" is a disease, disorder, syndrome, and the like; or a symptom thereof.

[0017] As used herein a "lipid imbalance" refers to a suboptimal/undesirable lipid profile in blood or other tissue of a mammal, or a deficiency or excess of one or more lipids as compared with a medical norm or as indicated by the manifestation of a disorder. It is understood that the body's defense mechanisms (such as storage of essential fatty acids among others) can help compensate for a deficiency or excess of a particular fatty acid to a limited extent.

[0018] As used herein a "therapeutically effective amount" is an amount of a composition that results in the prophylaxis and/or treatment of a medical condition or symptom of a medical condition. In some embodiments, the adverse level of a biomarker or the severity of a symptom of the medical condition is abated at least 10% or more, at least 25% or more, at least 50% or more, at least 75% or more, or 100% ameliorated.

[0019] As used herein the phrase "adequate amount of omega-3 fatty acids" refers to a minimum of dietary reference intake (DRI) levels of omega-3 fatty acids per day from foods, supplements, and/or the lipid compositions.

[0020] A "therapeutic effect," as that term is used herein, encompasses a therapeutic benefit and/or a prophylactic benefit. By therapeutic benefit is meant eradication or amelioration of the underlying disorder being treated. Also, a therapeutic benefit may be achieved with the eradication or amelioration of one or more of the physiological symptoms associated with the underlying disorder such that an improvement may be observed in the patient, notwithstanding that the patient may still be afflicted with the underlying disorder. For prophylactic benefit, the compositions may be administered to a patient/individual at risk of developing a particular disease, or to a patient/person reporting one or more of the physiological symptoms of a disease, even though a diagnosis of this disease may not have been made. A prophylactic effect includes delaying or eliminating the appearance of a disease or condition, delaying or eliminating the onset of symptoms of a disease or condition, slowing, halting, or reversing the progression of a disease or condition, or any combination thereof.

Lipid Formulations

[0021] In one aspect, the present disclosure incorporates relatively high ratio of omega-6 to omega-3 fatty acids, while maintaining optimal daily delivery of both omega-6 and omega-3 fatty acids. One reason for maintaining the high ratio is because of the incorporation of nuts, seeds, and nut oils as integral components of a formulation, which nuts, seeds, and nut oils have high antioxidants, mineral, and phytochemical content and other properties that may render excessive omega-3 unnecessary. In some instances, excessive omega-3 (which have 3 to 6 double bonds) may be associated with per-oxidative stress. Certain embodiments of the present disclosure may favor in-vivo formation of Linoleic acid metabolites Gamma-linolenic acid (3 double bonds) and Dihomo-gamma-linolenic acid (3 double bonds), which may have dose-dependent anti-inflammatory properties and other health benefits. Nuts and seeds may have a narrow therapeutic window, unfavorable interactions, and other properties requiring judicious use; therefore the formulations deliver measured and optimized quantities of nuts and seeds along with oils.

[0022] Certain embodiments of the present disclosure provide for compositions comprising supplementation with one or more of the following: vitamin A, B9 (folic acid), C, D, E; alkaloids, carotenoids, like beta-carotene, lycopene, astaxanthin, lutein, zeaxanthin; monophenols; polyphenols, flavonoids, stilbenes

such as resveratrol, flavonols such as quercetin, and kaempferol; flavanones; flavones; flavan-3-ols such as catechins; anthocyanins and anthocyanidins; isoflavones; phytoestrogens; phytotesterols such as campesterol, sitosterol, and stigmasterol; phenolic acids such as gallic acid, ellagic acid, and curcumin; hydroxycinnamic acids such as coumarins; organosulfides; saponins; terpenoids; lactones; melatonin; lignans; and antioxidants and phytochemicals in general. In certain embodiments, each of these supplements/nutrients may reduce/alter the requirement/tolerance for omega-3 fatty acids and allow for a higher omega-6 to omega-3 ratio than in the absence of said supplement(s)/nutrient(s). In certain embodiments, minerals and trace elements such as Na, K, Ca, Mg, Fe, Cu, Zn, Mn, and Se may also alter the metabolism and/or requirements/tolerance for omega-6 and omega-3 fatty acids. In certain embodiments, microorganisms/ probiotics may also alter the metabolism and/or requirements/tolerance for omega-6 and omega-3 fatty acids. In certain embodiments, each of the above nutrients is optimized through natural sources such as oils, butters, nuts, seeds, herbs, sweeteners, and other foods.

[0023] Nuts and seeds are plant embryos containing plant stem cells. They are made to survive the harshest of the climactic conditions until factors are suitable for germination. As such, gram per gram, they are one of the richest sources of natural nutrients. Almonds are one of the most nutritionally dense nuts, providing an array of powerful nutrients: flavonoids, vitamin E, manganese, magnesium, copper, vitamin B2 and phosphorus, to name a few. The flavonoids found in nuts, particularly almond skins, together with the vitamin E found in their meat double the antioxidants that either delivers separately.

[0024] Walnuts, pecans and chestnuts have the highest antioxidant content of the tree nuts, with walnuts delivering more than 20 mmol antioxidants per 3 ounces, including at least 16 antioxidant phenols, vitamin E, and ellagic and gallic acid. Walnuts are also exceptionally high in their content of the omega-6 fatty acid linoleic acid and the omega-3 fatty acid alpha-linolenic acid.

[0025] Peanuts also contribute significantly to dietary intake of antioxidants, rivaling the antioxidant content of blackberries and strawberries, and are far richer in antioxidants than apples, carrots or beets. Peanuts are a good source of vitamin E (gamma- and alpha- tocopherol), niacin, folate, proteins, and manganese. Peanuts

also contain high concentrations of phytochemicals polyphenols, including resveratrol.

[0026] Sesame seeds are a very good source of manganese, copper, calcium, magnesium, iron, phosphorus, vitamin B1, zinc and dietary fiber. In addition to these important nutrients, sesame seeds contain sesamin and sesamolin, lignans. Sesame seeds have the highest total phytosterol content (400-413 mg per 100 grams) of all nuts and seeds; pistachios and sunflower seeds are the second richest (270-289 mg/100 g), closely followed by pumpkin seeds (265 mg/100 g).

[0027] A quarter cup of sunflower seeds may provide 31.9% of the daily value for magnesium. Sunflower seeds are also a good source of selenium. Cashews, flaxseeds, pumpkin seeds, and sesame seeds are a good source of magnesium. Almonds, cashews, sunflower seeds, pumpkin seeds, walnuts, and sesame seeds are a good source of copper. Almonds, flaxseeds, peanuts, sunflower seeds, pumpkin seeds, and walnuts are a good source of manganese. Just one-quarter cup of almonds may supply 45.0% of the daily value for manganese, and 20.0% of the daily value for copper.

[0028] In one aspect, the disclosure provides compositions that include seeds, nuts, and/or oils. In another aspect the compositions include legumes, dairy, cocoa, lentils, and/or grains. In one embodiment the composition can include one or more edible oils, culinary nuts and/or seeds in their whole form or their oils such as, but not limited to acai oil, amaranth oil, apple seed oil, apricot kernel oil, argan oil, artichoke oil, avocado oil, babassu oil, ben oil, blackcurrant seed oil, borage seed oil, borneo tallow nut oil, bottle gourd oil, buffalo gourd oil, butter oil (anhydrous), canola oil (rapeseed), cape chestnut oil, carob pod oil, cocklebur oil, cocoa butter oil, cohune oil, coriander seed oil, corn oil, cottonseed oil, dika oil, evening primrose oil, false flax oil (camelina sativa), fish oil (cod liver), fish oil (herring), fish oil (menhaden), fish oil (salmon), fish oil (sardine), grapeseed oil, household lard, kapok seed oil, lallemantia oil, marula oil, meadowfoam seed oil, mustard oil, nutmeg butter, okra seed oil, palm oil. papaya seed oil, pequi oil, perilla oil, prune kernel oil, quinoa oil, ramtil oil, rice bran oil, royle oil, sacha inchi oil, safflower oil, sheanut oil, soybean lecithin oil, tea oil, thistle oil, tomato seed oil, ucuhuba butter oil, wheat germ oil, acorns, almonds, beech nuts, brazilnuts, breadnuts, candlenuts, chestnuts, chilacayote nuts, chilean hazel nuts, coconuts, cashews, colocynth nuts, filberts, hazelnut, hickory, kola nut,

macadamia, mamoncillo, melon seeds, mongongo, obongo nut, olives, peanuts, pecans, pili nuts, pine nuts, pistachios, soya nuts, poppy seeds, pumpkin seeds, hemp seeds, flax seeds, sesame seeds, sunflower seeds, walnuts, and watermelon seeds.

[0029] In some embodiments, the compositions of the present disclosure include the following optimally balanced fatty acids and combinations thereof. Saturated fatty acids: butyric (C4:0), lauric (C12:0), myristic (C14:0), palmitic (C16:0), stearic (C18:0), and arachidic (20:0); monounsaturated fatty acids: myristoleic (C14:1), palmitoleic (C16:1), and omega-9 oleic (C18:1), gadoleic (C20:1), erucic (C22:1), and nervonic (C24:1); and polyunsaturated fatty acids: omega-6 linoleic (C18:2), conjugated-linoleic (C18:2), gamma-linolenic (C18:3), eicosadienoic (C20:2), di-homo-gamma-linolenic (C20:3), and arachidonic (C20:4); and omega-3 alpha-linolenic (C18:3), stearidonic (C18:4), eicosapentaenoic (C20:5), docosapentaenoic (C22:5), and docosahexaenoic (C22:6) fatty acids.

[0030] In some embodiments, synergy among complementing nutrients from different sources may be incorporated. For example, in-vivo oxidation may take different pathways; use of optimal mix of antioxidants may be more effective in managing different pathways, providing for moderate level of oxidation necessary for physiology. Furthermore, using different sources avoids concentrated delivery of specific antioxidants and phytochemicals that may be harmful in excess (for example some phytosterols), since nuts and seeds are known to have strong positive and negative outcomes. In one embodiment, Ayurvedic principles (ancient Indian medicine proven empirically over centuries) around the use of oils, nuts, and seeds may be integrated with western molecular science to design various lipid-containing compositions.

[0031] Given below in Table 2 are some examples of components of oils. USDA website (http://www.nal.usda.gov/fnic/foodcomp/search/) can be consulted for detailed components of various oils, nuts and seeds.

Table 2. Relevant Components of Dietary Oils

		Peanut Oil	Corn Oil	Sunflower Oil (high linoleic)	Fish Oil (herring)	Butter Oil (Anhydrous)	Coconut Oil
Nutrient	**Units**	**1 tbsp**	**1 tbsp**	**1 tbsp**	**1 tbsp**	**1 tbsp**	**1 tbsp**
Total lipid (fat)	g	13.5	13.6	13.6	13.6	12.73	13.6
Total Saturated	g	2.281	1.761	1.401	2.895	7.926	11.764

Fatty Acids							
Total Monounsaturated Fatty Acids	g	6.237	3.75	2.652	7.693	3.678	0.789
Total Polyunsaturated Fatty Acids	g	4.32	7.436	8.935	2.122	0.473	0.245
Butyric Acid (C4:0)	g					0.413	
Caproic Acid (C6:0)	g					0.244	0.082
Caprylic Acid (C8:0)	g					0.142	1.02
Capric Acid (C10:0)	g					0.319	0.816
Lauric Acid (C12:0)	g				0.021	0.358	6.066
Myristic Acid(C14:0)	g	0.014	0.003		0.977	1.281	2.285
Palmitic Acid (C16:0)	g	1.282	1.439	0.802	1.592	3.349	1.115
Margaric Acid (C17:0)	g		0.009				
Stearic Acid (C18:0)	g	0.297	0.251	0.612	0.111	1.543	0.381
Arachidic Acid (C20:0)	g	0.189	0.059				
Behenic Acid (C22:0)	g	0.378					
Lignoceric Acid (C24:0)	g	0.121					
Palmitoleic Acid (C16:1)	g	0.014	0.016		1.311	0.285	
Oleic Acid (C18:1, n-9)	g	6.048	3.717	2.652	1.626	3.203	0.789
Gadoleic Acid (C20:1, n-9)	g	0.176	0.018		1.853		
Erucic Acid (C22:1, n-9)	g				2.803		
Linoleic Acid (C18:2, n-6)	g	4.32	7.278	8.935	0.156	0.288	0.245
Alpha-linolenic Acid (C18:3, n-3)	g		0.158		0.104	0.185	
Arachidonic Acid (C20:4, n-6)	g				0.039		
Eicosapentaenoic Acid (C20:5 n-3)	g				0.853		
Docosapentaenoic Acid (C22:5 n-3)	g				0.084		
Docosahexaenoic Acid (C22:6 n-3)	g				0.572		
Vitamin A, RAE	mcg					108	
Retinol	mcg					105	
Carotene, beta	mcg					25	
Vitamin A, IU	IU					393	
Vitamin E (alpha-tocopherol)	mg	2.12	1.94	5.59		0.36	0.01
Tocopherol, beta	mg	0.06					

Tocopherol, gamma	mg	2.15					0.03
Tocopherol, delta	mg	0.18					
Vitamin K (phylloquinone)	mcg	0.1	0.3	0.7		1.1	0.1
Phytosterols	mg	28	132	14			12

[0032] In a related aspect, the disclosure provides compositions that include polyunsaturated fatty acids, monounsaturated fatty acids, saturated fatty acids, including omega-3, omega-6, and omega-9 fatty acids. In some embodiments the composition is a liquid formulation. In other embodiments the composition is a solid formulation. In yet other embodiments the composition is a semi-solid formulation. In certain embodiments, the composition can substitute the unbalanced fats (cooking oils, fats, and the like) that are typically added to various food preparations and/or supplement fats contained in an individual's diet from other sources. In certain embodiments, in addition to normal lipid-containing ingredients, the disclosure may further comprise herbs, spices, sweeteners, and additives. In certain embodiments, lipid-free or low-lipid diet plans are developed to complement the composition. In certain embodiments, the entire diet is a composition, balanced with respect to fatty acids, antioxidants, phytochemicals, vitamins, and minerals. In some embodiments, the disclosure includes compositions wherein the ratios and daily delivery of omega-3, omega-6 and omega-9 and other fatty acids are in an amount sufficient to prevent the onset or progression of, protect from the severity of, or decrease a medical condition or disorder, or a symptom thereof. In particular embodiments, the compositions described herein are formulated with respect to one or more of an individual's factors including but not limited to diet, gender, age categories such as infants, babies, children, adolescent, and adults, size, weight, physical activity, medical conditions, family medical history, climate and other demographic factors. In case of infants and babies the compositions may be formulated with respect to the mother's factors. The compositions may be delivered by any acceptable delivery method; in certain embodiments vitamins and minerals may be added to the compositions, and in certain embodiments, an additional vitamin and mineral supplement may be administered.

[0033] In one embodiment, an individual with a herbivorous diet, an ovo-lacto vegetarian diet, a vegan diet, or a high-antioxidant high-phytochemical omnivorous diet may be administered related compositions. In another aspect, an individual with a low-

antioxidant low-phytochemical herbivorous diet, a low-antioxidant low-phytochemical ovo-lacto vegetarian diet, a low-antioxidant low-phytochemical vegan diet, or a low-antioxidant low-phytochemical omnivorous diet may be administered related compositions. In another aspect, an individual may be administered with compositions that are formulated with respect to whether his or her diet comprises a low or high intake of seafood. This pertains to concentrated lipid compositions. One method of measuring antioxidant and phytochemical consumption is to measure the number of fruits, vegetables, whole grains, and legumes servings per day, where two or more per day may provide high-antioxidant, high-phytochemical content. However, two or more servings of foods such as white rice or potatoes may contain very little phytochemicals. Yet certain other foods, particularly herbs such as turmeric, may contain potent phytochemicals (even in small quantities, e.g., a quarter-teaspoon). The websites www.phytochemicals.info and http://www.ars-grin.gov/duke/ may be consulted for additional information on phytochemicals. Therefore, the disclosure provides a number of different compositions, including one with varying levels of omega-3 fatty acids to suit a consumer's diet and/or tolerance level. As used herein, "tolerance" and the like mean the ability of a consumer to withstand the composition without any discomfort. In some embodiments, the compositions designed for consumers with high seafood diet (two or more seafood servings per week), include low amount of nuts and seeds. In some instances, no nuts or seeds are included. Other phytochemicals may also be minimized or eliminated as part of a composition to avoid unfavorable interactions. The method is shown schematically in Table 3.

Table 3. Schematic representation for developing tailored dietary lipid programs and for optimizing dietary nutrients

1. Develop dietary cohorts[a,b]

	High phytochemicals	High meat	High seafood
Grains			
Brown Rice	--to-- cups/g	--to-- cups/g	--to-- cups/g
Whole	--to-- cups/g	--to-- cups/g	--to-- cups/g
Other	--to-- cups/g	--to-- cups/g	--to-- cups/g
Vegetables	Develop ranges as above		
Fruits	Develop ranges as above		
Legumes	Develop ranges as above		
Dairy	Develop ranges as above		
Meats	Develop ranges as above		
Seafood	Develop ranges as above		
Herbs	Develop ranges as above		
Sweeteners	Develop ranges as above		
Beverages	Develop ranges as above		

2. Compute range of nutrients

Lipids			
C4:0	--to-- mg	--to-- mg	--to-- mg
C22:6 w3	--to-- mg	--to-- mg	--to-- mg
Other	--to-- mg	--to-- mg	--to-- mg
Carbohydrates	Compute ranges as above		
Protein	Compute ranges as above		
Vitamins	Compute ranges as above		
Minerals	Compute ranges as above		
Phytochemicals	Compute ranges as above		
Antioxidants	Compute ranges as above		

3. Develop lipid programs

Develop lipid programs to complement the nutrients above, from natural oils, nuts, seeds, and herbs; additional vitamins and minerals may be used. Deliver as diurnal mutually complementing individual dosages; daily variety may strengthen compliance

Monday	Oil blend-A +	sauce-A +	spread-A +	dessert-A
Tuesday	Oil blend-B +	sauce-B +	spread-B +	dessert-B
Other	Oil blend-X +	sauce-X +	spread-X +	dessert-X

[a]Based on average daily consumption.

[b]Further customizations may address age, gender, climactic temperature, and medical conditions/ lipid tolerance.

Administration

[0034] In some embodiments, the compositions comprising the lipid formulation disclosed herein may be administered to an individual in any orally accepted form. The lipid formulations may be packaged in one, two, three, four or more mutually complementing daily dosages. In some embodiments, they may be contained in any one or more of, but not limited to, a single dosage or sustained and controlled release capsule, soft-gel capsule, hard capsule, tablet, powder, lozenge, or pill prepared in some instances with carriers such as starches, sugars, diluents, granulating agents, lubricants, binders, disintegrating agents, and the like; a

powder such as infant formula or a granule; a baby food; a nutritional bar; a bakery food product such as a bread, a dessert, a pastry, a truffle, a pudding or cake; a sealed single dosage packet or resealable packaging containing a liquid, an oil blend, a gel, a sauce, a dressing, a spread, a butter, drops, a semi-solid; liquid, or the like; or a cooking oil such as a frying oil, a pan-frying oil, a parting oil or the like. In some embodiments, they may be unsealed and taken orally, or added as part of a cooking ingredient to previously cooked or uncooked food preparation with or without added fat. For example, they can be made into special cooking oil, butter, dressing, etc. and be added into foods while such foods are being prepared. In certain embodiments, some or all of the components of the compositions may be skinned and/or unskinned, pre-soaked and/or un-soaked, sprouted and/or un-sprouted, cut and/or uncut, diced, shredded, pureed, grinded, blended, grilled, baked, roasted, sautéed, and/or cooked or uncooked, unprocessed and/or processed by any other method. The components of the compositions may be delivered in one-part or multiple parts as various components of a meal or to complement a meal, for example. In some embodiments, the lipid-containing compositions may be delivered using a gelatinous case, a vial, a pouch or a foil for containing such compositions. In some embodiments, they may be part of an enteral or parenteral formula, or a combination thereof. In some embodiments a one-day, one-week, two-week, bi-weekly, bi-monthly, or monthly diet plan may be formulated comprising various lipid formulations described herein, with varying compositions administered each day.

[0035] The balanced lipid composition disclosed herein may be used to create a completely balanced diet plan, by adding the composition, which contains balanced components of lipids, phytochemicals, antioxidants, vitamins, and minerals to name a few, into foods as a dietary component. In one embodiment, a dietary component can be a cooking ingredient added to prepared or unprepared food or beverage. In some embodiments, it can also be a finished food product such as a dessert or side dish, which are served together with other components of a meal. Special foods containing no lipid or low lipids (for example small amounts of lipids contained in meats, poultry, seafood, milk, fruits, vegetables, legumes and grains) may be created to be used together with balanced lipid formulation to ensure the complete balance of the lipid intake. Again, the administration of the balanced composite nutrients may be achieved through one

course in a meal or multiple courses in a meal (e.g., salad, main course, and dessert).

[0036] Each individual may be given instructions on use of the product, and risk and cautionary measures, as is usual with any pharmaceutical, nutraceutical, or any product intended for ingestion. Oils, nuts, seeds, and herbs are potent; therefore, instructions may include recommended dosage, frequency, and suggestions for optimization. For example, sesame seeds, particularly in large amounts may induce uterine contractions, and therefore pregnant women may be cautioned against the use of certain compositions comprising sesame seeds before full-term; such compositions however may be beneficial for certain other conditions.

[0037] The delivery of the desired lipid composition may be achieved through a one-part or multi-part mutually complementing delivery system. For example, the desired formulation may be achieved through adding various components to various parts of a meal, including bread, salad, main course, and/or dessert.

[0038] One aspect of the disclosure is to deliver fatty acids in such a way that the total daily delivery of omega-6 and omega-3 from the lipid composition and the rest of the diet are optimal with respect to daily recommendations.

[0039] Yet another aspect of the present disclosure is the concept of steady delivery of fatty acids, with respect to phytochemicals, antioxidants, and minerals, based on the observation that each time there is a change in dietary lipid delivery/consumption, it upsets the body physiology, sometimes with adverse effects such as headaches, muscle and joint pains, digestive and bowel upset, mental confusion, and anxiety; and at other times it may cause short-lived euphoria and general sense of wellness. Though the body adapts to the change in 2-3 weeks or longer, long-term effects of the change/consumption outside the optimal range may be harmful. Furthermore, sudden large fluctuations in fatty acids ingestion can also have acute adverse effects. Sudden withdrawal of a habitual high long-chain omega-3 fatty acids or immunosuppressive phytochemical/nutrient supply from the host, or sudden increase in omega-6 fatty acids may result in release of a cytokine storm, with severe consequences involving systemic inflammatory response (capillary leakage, pyrexia, tachycardia, tachypnoea), multi-organ dysfunction (gastrointestinal, lungs, liver, kidney, heart), and connective tissue damage in the joints. At such instances the host may be most vulnerable to infections, myocardial infarction, stroke, and

induction of psoriasis depending upon the rest of the body chemistry and the presence of infectious agents. In less severe manifestations, due to moderate fluctuations in fatty acids and in otherwise salubrious condition, the host may experience sleep disturbance, headaches, muscle cramps, confusion, melancholia, and rage resulting from changes in neurotransmission, excitability of muscle and neural cells, fluctuating eicosanoids, and androgens. This steady delivery requires a steady dosage within the optimal range lasting approximately 2 to 3 weeks at a minimum.

EXAMPLES

Example 1. Formulas with Various Lipid Ratios

[0040] In specific embodiments of the disclosure the formulations described herein have high antioxidant and phytochemical content and properties that render extra omega-3 unnecessary. In specific embodiments lignans (such as in sesame), sweeteners (such as honey), and herbs/spices (such as turmeric) included in the compositions can render extra omega-3 unnecessary. The formulations may provide a balanced fatty acid composition of approximately 10-100 grams of total daily fat. The formulations may include specific ratios of various lipid components as shown below in Table 4. The ratios may be weight by weight, weight by volume, or volume by volume (w/w, w/v, or v/v).

Table 4. Lipid Ratios

Lipid Component Ratio	Approximate Ratio Range
Omega-6 to Omega-3 Fatty Acids	1:1 - 50:1
Omega-9 to Omega-6 Fatty Acids	0.5:1 - 6:1
Total Fatty Acids to Monounsaturated Fatty Acids	1:1 - 15:1
Monounsaturated to Polyunsaturated Fatty Acids	0.25:1 - 6:1
Monounsaturated to Saturated Fatty Acids	0.25:1 – 7:1
Total Fatty Acids to Polyunsaturated Fatty Acids	1:1 -15:1
Total Fatty Acids to Saturated Fatty Acids	1:1 -15:1

[0041] In some embodiments, the lipid formulation calls for specific percentages of omega-9, omega-6, and omega-3 fatty acids, as shown in Table 5 below.

Table 5. Contents of Various Unsaturated Fatty Acids

Lipid Name	Content (w/w, w/v, or v/v of total lipids)
Omega-9	10-90%
Omega-6	4-75%
Omega-3	0.1-30%
Vitamin E-alpha/gamma	0.001-0.5%

Example 2. Lipid Compositions According to Climate

[0042] In one embodiment, compositions of the disclosure are formulated as per climatic condition and ambient temperature range. Table 6 provides % by weight ranges for a lipid formulation that includes oils, nuts and seeds as disclosed by embodiments of the present disclosure, by climatic condition and temperature range.

Table 6. Lipid Formulation According to Climate

% by Weight Ranges by Temperature (in °F)	HOT 90°- 135°		WARM 70°- 99°		COOL 50°- 75°		COLD 33°- 55°		BELOW FREEZING 0°- 37°		ARCTIC -50°- 5°		POLAR -100°- -45°	
	Low	High	Low	High	Low	High	Low	High	Low	High	Low	High	Low	High
Oils														
Anhydrous Butter Oil	2	36	2	30	1	29	2	28	2	30	2	30	2	30
Avocado Oil	0	15	0	15										
Coconut Oil	0	25												
Corn Oil			0	15	0	15	0	15	2	30	2	30	2	30
Cotton seed oil	0	15	0	15	0	15	0	15	0	15	0	15	0	15
Fish Oil			0	15	0	15	0	15	0	20	0	20	0	20
Grapeseed oil	0	15	0	15	0	15	0	15	0	15	0	15	0	15
Hemp oil	0	15	0	15	0	15	0	15	0	15	0	15	0	15
Mustard Oil					0	15	0	15	0	20	0	20	0	20
Olive Oil			1	30	1	29	2	30	2	30	4	60	4	60
Palm Oil			0	5	0	5	0	5	0	5	0	5	0	1
Peanut Oil	2	68	2	53	0	35								
Perrilla oil	0	15	0	15	0	15	0	15	0	15	0	15	0	15
Rapeseed Oil	0	15	0	15	0	15	0	30	2	30	0	30	0	30
Rice Bran Oil	0	15	0	15	0	15	0	15	0	15	0	15	0	15
Safflower Oil	2	68	2	53	1	29	2	30	2	30	2	30	2	30
Soybean Lecithin	0	2	0	2	0	2	0	2	0	2	0	2	0	1
Sunflower Oil	4	72	2	53	1	37	2	30	2	30	2	30	2	30
Wheatgerm oil					0	10	0	10	0	10	0	10	0	10

Nuts and Seeds														
Almonds	3	48	3	49	2	47	3	46	3	48	3	48	3	48
Brazilnut					0	10	0	15	0	15	0	15	0	15
Cashews	2	37	2	31	1	20	1	18						
Chestnut							0	15	0	15	0	15	0	15
Coconut	0	25	0	10	0	10	0	5	0	5	0	5	0	4
Flaxseed					0	20	0	15	1	10	0	17	0	17
Hazelnut					0	10	0	15	0	15	0	15	0	15
Macadamia Nuts					0	10	0	15	0	15	0	15	0	15
Olives	2	33	2	28	1	28	2	27	2	28	2	28	2	28
Peanuts					1	33	2	38	3	47	3	47	3	47
Pine nuts							0	15	0	15	0	15	0	15
Pistachios			1	20	1	17	1	15	1	14	0	14	0	14
Pumpkin seeds	3	54	3	46	2	45	3	43						
Sesame					0	10	0	15	0	15	0	15	0	15
Soybeans			2	34	1	34	2	33	2	34	2	34	2	34
Sunflower Seeds	1	15	1	15	0	10	1	10						
Walnuts	2	33	2	28	1	27	2	26	2	27	2	27	2	27

[0043] Table 7 provides % by weight ranges (% of weight of the entire composition) for omega-9, omega-6, and omega-3 fatty acids as disclosed by embodiments of the present disclosure, by climatic condition and temperature range.

Table 7. Unsaturated Fatty Acid Contents According to Climate

% by Weight Ranges by Temperature (in °F)	**HOT** 90°- 135°		**WARM** 70°- 99°		**COOL** 50°- 75°		**COLD** 33°- 55°		**BELOW FREEZING** 0°- 37°		**ARCTIC** -50°- 5°		**POLAR** -100°- -45°	
	Low	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**
Omega-9 Fats	20	90	20	90	20	90	10	80	10	80	10	80	10	80
Omega-6 Fats	4	60	4	60	6	60	10	60	12	70	13	70	15	73
Omega-3 Fats	0.3	5	0.5	6	0.8	7	1	8	1.5	12	1.8	15	2	20

[0044] In the following example, specific lipid compositions were prepared for healthy individuals living in a variety of climates, with a high antioxidant/phytochemical diet and/or a vegetarian diet, for maintenance of general health and well-being. The compositions were made up of a variety of oils, nuts and seeds, as described in Table 6. The compositions presented in Table 8 were formulated by three different methods: lipid liquid formulation only, a solid or semi-solid nut and seed formulation only, or a combination formulation containing oils, nuts and seeds. The compositions were formulated to be administered in a once a day format (combined formulation), or a twice a day format where one administration was of

the liquid lipid formation and the other administration was of the solid nut and seed composition.

[0045] Table 8 provides the omega-6 to omega-3 ratio contained in the lipid compositions of this example for a range of climates. The ratios are presented, for any one of the liquid only, solid only, or combination formulations.

Table 8. Ratio of Omega-6 (O6) to Omega-3 (O3) by Climate

	O6:O3 Ratio by Climate (°F)
Hot: 90°- 135°	20:1
Warm: 70°- 99°	18:1
Cool: 50°-75°	15:1
Cold: 33°- 55°	13:1
Below Freezing: 0°- 37°	10:1
Arctic: -50°- 5°	8:1
Polar: -100°- -45°	7:1

[0046] Table 9 provides the ratio of total lipids to each of monounsaturated, polyunsaturated, and saturated fatty acids in the lipid compositions of this example, for a range of climates. The ratios are presented, for any one of the liquid only, solid only, or combination formulations.

Table 9. Ratio of Total Lipids to Specific Lipid Components By Climate

Ratios by Climate (°F)	**HOT**	**WARM**	**COOL**	**COLD**	**BELOW FREEZING**	**ARCTIC**	**POLAR**
	90°- 135°	**70°- 99°**	**50°- 75°**	**33°- 55°**	**0°- 37°**	**-50°-5°**	**-100°- -45°**
Total Lipids: Monounsaturated Fats	2.1	2.2	2.2	2.1	2.2	2.1	2.1
Total Lipids: Polyunsaturated Fats	3.8	3.2	3.2	3.3	3.1	3.3	3.2
Total Lipids: Saturated Fats	5.0	5.4	5.5	5.7	5.9	6.1	6

Example 3. Lipid Compositions Based on Age, Sex and Diet

[0047] One aspect of the disclosure is to supply lipid formulation tailored to different human subjects based on their age and sex, and diet. Table 10 below provides dose ranges for total fatty acids content in grams, the ratio range of monounsaturated fatty acids to polyunsaturated fatty acids, and the ratio range of monounsaturated fatty acids to saturated fatty acids, range of omega-6 fatty acids

content in grams, ratio range of omega-9 to omega-6 fatty acids, range of omega-3 fatty acids content in grams, and the ratio range of omega-6 to omega-3 fatty acids for vegetarian or high antioxidant and/or high phytochemical consuming non-vegetarian subjects as disclosed by embodiments of the present disclosure, by gender and age group.

Table 10. Lipid Dosages Based on Age and Sex for Vegetarians and High Anti-Oxidant/Phytochemical Consuming Omnivores

	Range Total Fat - g	Range Mono:Poly	Range Mono:Sat	Range O6 - g	Range O9:O6	Range O3 - g	Range O6:O3
Infants							
7-12 mo	10-50	1:1-3:1	1:1-5:1	1-10	1:1-3:1	0.1-3	4:1-45:1
Children							
1-3 y	10-60	1:1-3:1	1:1-5:1	2-15	1:1-3:1	0.1-3	4:1-45:1
Males							
4-8 y	10-75	1:1-3:1	1:1-5:1	2-25	1:1-3:1	0.1-4	4:1-45:1
9-13 y	15-80	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.1-4	4:1-45:1
14-18 y	20-100	1:1-3:1	1:1-5:1	2-35	1:1-3:1	0.2-5	4:1-45:1
19-30 y	20-100	1:1-3:1	1:1-5:1	2-40	1:1-3:1	0.2-5	4:1-45:1
31-50 y	20-80	1:1-3:1	1:1-5:1	2-40	1:1-3:1	0.2-5	4:1-45:1
51-70 y	15-80	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.2-5	4:1-45:1
>70 y	15-80	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.2-5	4:1-45:1
Females							
4-8 y	12-70	1:1-3:1	1:1-5:1	2-25	1:1-3:1	0.1-3	4:1-45:1
9-13 y	15-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	0.1-3	4:1-45:1
14-18 y	20-80	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.2-4	4:1-45:1
19-30 y	20-80	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.2-4	4:1-45:1
31-50 y	15-80	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.2-4	4:1-45:1
Pregnancy	24-100	1:1-3:1	1:1-5:1	2-35	1:1-3:1	0.2-5	4:1-45:1
Lactation	24-100	1:1-3:1	1:1-5:1	2-35	1:1-3:1	0.2-5	4:1-45:1
Menopause	15-80	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.2-4	4:1-45:1

[0048] Table 11 provides dose ranges for total fatty acids content in grams, the ratio range of monounsaturated fatty acids to polyunsaturated fatty acids, and the ratio range of monounsaturated fatty acids to saturated fatty acids, range of omega-6 fatty acids content in grams, ratio range of omega-9 to omega-6 fatty acids, range of omega-3 fatty acids content in grams, and the ratio range of omega-6 to omega-3 fatty acids for non-vegetarian (i.e., omnivorous) or low-antioxidant and/or low phytochemicals consuming vegetarian subjects as disclosed by the present disclosure by gender and age group.

Table 11. Lipid Dosages Based on Age and Sex for Omnivores and Low Anti-Oxidant/Phytochemical Consuming Vegetarians

Range Total	Range Mono:Poly	Range	Range	Range O9:O6	Range	Range

	Fat - g		Mono:Sat	O6 - g		O3 - g	O6:O3
Infants							
7-12 mo	10-50	1:1-3:1	1:1-5:1	1-10	1:1-3:1	0.1-3	1:1-10:1
Children							
1-3 y	10-60	1:1-3:1	1:1-5:1	2-15	1:1-3:1	0.1-3	1:1-10:1
Males							
4-8 y	10-75	1:1-3:1	1:1-5:1	2-20	1:1-3:1	0.2-5	1:1-10:1
9-13 y	15-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	0.2-5	1:1-10:1
14-18 y	20-100	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.3-6	1:1-10:1
19-30 y	20-100	1:1-3:1	1:1-5:1	2-35	1:1-3:1	0.3-6	1:1-10:1
31-50 y	20-80	1:1-3:1	1:1-5:1	2-35	1:1-3:1	0.3-6	1:1-10:1
51-70 y	15-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	0.3-6	1:1-10:1
>70 y	15-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	0.3-6	1:1-10:1
Females							
4-8 y	12-70	1:1-3:1	1:1-5:1	2-20	1:1-3:1	0.2-4	1:1-10:1
9-13 y	15-80	1:1-3:1	1:1-5:1	2-20	1:1-3:1	0.2-4	1:1-10:1
14-18 y	20-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	0.3-5	1:1-10:1
19-30 y	20-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	0.3-5	1:1-10:1
31-50 y	15-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	0.3-5	1:1-10:1
Pregnancy	24-100	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.3-5	1:1-10:1
Lactation	24-100	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.3-5	1:1-10:1
Menopause	15-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	0.3-5	1:1-10:1

[0049] Table 12 provides dose ranges for total fatty acids content in grams, the ratio range of monounsaturated fatty acids to polyunsaturated fatty acids, and the ratio range of monounsaturated fatty acids to saturated fatty acids, range of omega-6 fatty acids content in grams, ratio range of omega-9 to omega-6 fatty acids, range of omega-3 fatty acids content in grams and the ratio range of omega-6 to omega-3 fatty acids for high-seafood consumers as disclosed by the present disclosure by gender and age group.

Table. 12. Lipid Dosages Based on Age and Sex for High-Seafood Consumers

	Range Total Fat - g	Range Mono : Poly	Range Mono : Sat	Range O 6 - g	Range O9 : O6	Range O3 - g	Range O6 : O3
Infants							
7-12 mo	10-50	1:1-3:1	1:1-5:1	1-10	1:1-3:1	0.1-3	2:1-30:1
Children							
1-3 y	10-60	1:1-3:1	1:1-5:1	2-15	1:1-3:1	0.1-3	2:1-30:1
Males							
4-8 y	10-75	1:1-3:1	1:1-5:1	2-25	1:1-3:1	0.1-4	2:1-30:1
9-13 y	15-80	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.1-4	2:1-30:1
14-18 y	20-100	1:1-3:1	1:1-5:1	2-35	1:1-3:1	0.2-5	2:1-30:1
19-30 y	20-100	1:1-3:1	1:1-5:1	2-40	1:1-3:1	0.2-5	2:1-30:1
31-50 y	20-80	1:1-3:1	1:1-5:1	2-40	1:1-3:1	0.2-5	2:1-30:1
51-70 y	15-80	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.2-5	2:1-30:1
>70 y	15-80	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.2-5	2:1-30:1
Females							
4-8 y	12-70	1:1-3:1	1:1-5:1	2-25	1:1-3:1	0.1-3	2:1-30:1

9-13 y	15-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	0.1-3	2:1-30:1
14-18 y	20-80	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.2-4	2:1-30:1
19-30 y	20-80	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.2-4	2:1-30:1
31-50 y	15-80	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.2-4	2:1-30:1
Pregnancy	24-100	1:1-3:1	1:1-5:1	2-35	1:1-3:1	0.2-5	2:1-30:1
Lactation	24-100	1:1-3:1	1:1-5:1	2-35	1:1-3:1	0.2-5	2:1-30:1
Menopause	15-80	1:1-3:1	1:1-5:1	2-30	1:1-3:1	0.2-4	2:1-30:1

Example 4. Diet Formulations

[0050] In one embodiment, the total daily lipids from all foods are within the ratios described herein and the compositions described herein are administered to an individual that falls within the age and calorie intake range as recommended.

[0051] In another embodiment, the lipid ratios and compositions described herein are administered to an individual whose total diet comprises 20%-45% of calories from fat (including from the lipid compositions), 45%-65% calories from carbohydrates, and 10%-25% calories from proteins. In one particular aspect, the total calories consumed by the individual falls within the ranges as daily recommended average, as per gender, age, and activity level, to name a few.

[0052] In particular embodiments a meal plan may be established for the subject to be followed in conjunction with the administration of the composition.

[0053] In some embodiments, the lipid ratios and compositions described herein are administered to an individual whose diet comprises 20%-45% of calories from fat. In one aspect 50-90% of calories from fat are supplied by the lipid compositions described herein. In a further aspect the calories from fats are supplied by one or more of fish oils, dairy products (butter, butter oil, milk, milk cream, and/or cheese), fruit oils, vegetable oils, nuts, seeds, nut oils, and seed oils.

[0054] In some embodiments, the lipid ratios and compositions described herein are administered to an individual whose diet comprises 45%-65% of total calories from carbohydrates. In another aspect the diet comprises 45%-65% of total calories from carbohydrates, which carbohydrates are from a 50%-70% intake of grains in calories, 15%-30% intake of vegetables in calories, and 10%-30% intake of fruits in calories. In a related aspect the calories from carbohydrates are additionally from one or more of spices, sweeteners, and beverages. In a further aspect the 50%-70% of carbohydrates from grains are supplied by one or more of wheat, rice, corn, barley, spelt, oats, rye, buckwheat, millet, quinoa, and other grains.

[0055] In some embodiments, the lipid ratios and compositions described herein are administered to an individual whose diet comprises 10%-25% of calories from proteins. In another aspect the diet comprises 10%-25% of calories from proteins, which proteins are from one or more of but not limited to legumes, eggs, cheese, milk, yogurt, poultry, seafood, and meat.

[0056] In one embodiment, a diet plan is provided which includes the 20%-45% of calories from fat, which are supplied by the lipid compositions described herein. In a related embodiment, a 1-day, a 1-week, a 2-week, or a 1-month diet plan is provided which includes the 20%-45% of calories from fat, of which 50-90% of fat calories are supplied by the lipid compositions described herein. In one diet plan, the remaining 45-65% of calories from carbohydrates and 10-25% of calories from proteins are supplied by a diet including the following components, ranges specified in calories.

a. Calories from Carbohydrates 45-65%

i. Grains 50-70%
   1. Wheat <50%
   2. Rice <50%
   3. Corn <20%
   4. Barley <20%
   5. Spelt <20%
   6. Oats <20%
   7. Rye <20%
   8. Buckwheat <15%
   9. Millet <15%
   10. Quinoa <15%
   11. Other Grains <10%

ii. Vegetables 15-30%
   1. Asparagus, Bell Peppers, Cucumber, Eggplant, Green beans, Green peas, Kale, Romaine, Spinach, Squash summer and winter, Tomato, Carrots, Romaine Lettuce, Radish, Bitter Gourd, Okra, Fenugreek Leaves <50%
   2. Broccoli, Brussels Sprout, Cabbage, Chard, Cauliflower, Mustard Greens, Collard Greens, Turnip Greens <40%
   3. Turnip, Beets, Potatoes, Yams, Sweet Potatoes <50%
   4. Fungi, including mushrooms and yeast <25%
   5. Other Vegetables <15%

iii. Fruits 10-30%
   1. Apple, Apricot, Orange, Pear, Plum, Banana, Cantaloupe, Grapes <75%
   2. Grapefruit, Papaya, Mango, Pineapple <50%

3. Blueberries, Cranberries, Figs, Kiwi, Prune, Raspberries, Pomegranate, Strawberries, Watermelon <30%
4. Other fruits <15%

iv. Spices/Herbs <7%
1. Basil, Black pepper, Cayenne pepper, Chili Pepper, Cinnamon, Cloves, Coriander seeds and leaves, Cumin, Dill, Ginger, Mustard Seeds, Oregano, Peppermint leaves, Rosemary, Sage, Thyme, Turmeric, Fennel, Garlic, Onion, Leeks, Parsley, Celery, Cardamom, Saffron, Lime, Lemon, Tamarind, Table salt, Mint, Vinegar, other

v. Sweeteners <7%
1. Molasses, Cane Juice, Honey, Maple Syrup, Dates, Raisins, Dried Berries, Figs, Sugar, other

vi. Beverages <5%
1. Green tea, Black tea, Cocoa, Coffee, Alcohol, other <5%

b. Calories from proteins 10-25%

i. Legumes: Black beans, Dried Peas, Mung beans, Garbanzo, Kidney beans, Lentils, Lima beans, Navy beans, Pinto beans, Soybeans <75%
ii. Eggs <25%
iii. Cheese <25%
iv. Milk <25%
v. Yogurt <25%
vi. Poultry <30%
vii. Seafood <30%
viii. Meat <30%
ix. Other <15%

Example 5. Formulation with Varied Omega-3 Fatty Acid Content

[0057] Table 13 provides dose ranges for total fatty acids content in grams, the ratio range of monounsaturated fatty acids to polyunsaturated fatty acids, and the ratio range of monounsaturated fatty acids to saturated fatty acids, range of omega-6 fatty acids content in grams, ratio range of omega-9 to omega-6 fatty acids, ratio range of omega-6 to omega-3 fatty acids, range of omega-3 fatty acids content in grams designed by age and gender with increasing strength of omega-3, low, medium, and high, such that the human subject may choose the composition most agreeable to his/her diet, where the selection may be based upon the level of antioxidants and phytochemicals in the diet and/or medical predisposition.

Table 13. Lipid Dosages Based on Age and Sex for Various Levels of Omega-3 Fatty Acids

	Range Total Fat - g	Range Mono:Poly	Range Mono:Sat	Range O6 - g	Range O9:O6	Range O6:O3	Low Strength Range O3 - g	Med. Strength Range O3 - g	High Strength Range O3 - g
Infants									
7-12 mo	10-50	1:1-3:1	1:1-5:1	1-10	1:1-3:1	1:1-45:1	0.1-1.2	1.0-2.5	2.0-3.0
Children									
1-3 y	10-60	1:1-3:1	1:1-5:1	2-15	1:1-3:1	1:1-45:1	0.1-1.2	1.0-2.5	2.0-3.0
Males									
4-8 y	10-75	1:1-3:1	1:1-5:1	2-20	1:1-3:1	1:1-45:1	0.1-1.2	1.0-2.5	2.0-5.0
9-13 y	15-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	1:1-45:1	0.1-1.2	1.0-2.5	2.0-5.0
14-18 y	20-100	1:1-3:1	1:1-5:1	2-30	1:1-3:1	1:1-45:1	0.2-1.2	1.0-2.5	2.0-6.0
19-30 y	20-100	1:1-3:1	1:1-5:1	2-35	1:1-3:1	1:1-45:1	0.2-1.2	1.0-2.5	2.0-6.0
31-50 y	20-80	1:1-3:1	1:1-5:1	2-35	1:1-3:1	1:1-45:1	0.2-1.2	1.0-2.5	2.0-6.0
51-70 y	15-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	1:1-45:1	0.2-1.2	1.0-2.5	2.0-6.0
>70 y	15-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	1:1-45:1	0.2-1.2	1.0-2.5	2.0-6.0
Females									
4-8 y	12-70	1:1-3:1	1:1-5:1	2-20	1:1-3:1	1:1-45:1	0.1-1.2	1.0-2.5	2.0-4.0
9-13 y	15-80	1:1-3:1	1:1-5:1	2-20	1:1-3:1	1:1-45:1	0.1-1.2	1.0-2.5	2.0-4.0
14-18 y	20-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	1:1-45:1	0.2-1.2	1.0-2.5	2.0-5.0
19-30 y	20-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	1:1-45:1	0.2-1.2	1.0-2.5	2.0-5.0
31-50 y	15-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	1:1-45:1	0.2-1.2	1.0-2.5	2.0-5.0
Pregnancy	24-100	1:1-3:1	1:1-5:1	2-30	1:1-3:1	1:1-45:1	0.2-1.2	1.0-2.5	2.0-5.0
Lactation	24-100	1:1-3:1	1:1-5:1	2-30	1:1-3:1	1:1-45:1	0.2-1.2	1.0-2.5	2.0-5.0
Menopause	15-80	1:1-3:1	1:1-5:1	2-25	1:1-3:1	1:1-45:1	0.1-1.2	1.0-2.5	2.0-4.0

Example 6. Formulation Based on Medical Conditions

[0058] In various embodiments, lipid compositions described herein are administered to an individual for the prophylaxis and/or treatment of diseases, disorders or conditions. For example, the lipid formulation is used to alleviate symptoms of menopause, the process of the cessation of menstruation. It is also used to alleviate the symptoms of endocrine disorders.

[0059] Table 14 provides dose ranges for total fatty acids content in grams, the ratio range of monounsaturated fatty acids to polyunsaturated fatty acids, and the ratio range of monounsaturated fatty acids to saturated fatty acids, range of omega-6 fatty acids content in grams, ratio range of omega-9 to omega-6 fatty acids, range of omega-3 fatty acids content in grams, and the ratio range of omega-6 to omega-3 fatty acids for subjects with medical indications as disclosed by the present disclosure.

Table 14. Lipid Formulation Based on Medical Conditions

	Range Total Fat - g	Range Mono:Poly	Range Mono:Sat	Range O6 - g	Range O9:O6	Range O3 - g	Range O6:O3
Menopause	15-100	1:1-3:1	1:1-5:1	2-30	1:1-5:1	0.2-4	1:1-45:1
Cardiovascular Disease	15-100	1:1-3:1	1:1-5:1	2-35	1:1-5:1	0.1-6	1:1-45:1
Mental Disorders	15-100	1:1-3:1	1:1-5:1	2-30	1:1-5:1	0.1-6	1:1-45:1
Musculoskelatal Disorders	15-100	1:1-3:1	1:1-5:1	2-30	1:1-5:1	0.1-6	1:1-45:1
Symptoms of Aging	15-100	1:1-3:1	1:1-5:1	2-30	1:1-5:1	0.1-6	1:1-45:1
Endocrine Disorders	15-100	1:1-3:1	1:1-5:1	2-35	1:1-5:1	0.1-5	1:1-45:1
Viral Infections	15-100	1:1-3:1	1:1-5:1	1-30	1:1-5:1	0.1-4	1:1-45:1
Bacterial Infections	15-100	1:1-3:1	1:1-5:1	1-30	1:1-5:1	0.1-4	1:1-45:1
Obesity	15-100	1:1-3:1	1:1-5:1	1-40	1:1-5:1	0.1-6	1:1-45:1
Renal Diseases	15-100	1:1-3:1	1:1-5:1	1-30	1:1-5:1	0.1-6	1:1-45:1
Pulmonary Disorders	15-100	1:1-3:1	1:1-5:1	1-25	1:1-5:1	0.1-6	1:1-45:1
Opthalmologic Disorders	15-100	1:1-3:1	1:1-5:1	1-25	1:1-5:1	0.1-6	1:1-45:1
Dental Disorders	15-100	1:1-3:1	1:1-5:1	2-30	1:1-5:1	0.1-6	1:1-45:1
Cancer	15-100	1:1-3:1	1:1-5:1	1-35	1:1-5:1	0.1-6	1:1-45:1

Example 7. Lipid Composition According to Diet and Medical Condition

[0060] In one example lipid composition parameters were established per diet or medical condition, intended for daily administration (one or more components). As per Table 15 and Table 16 the parameters of the compositions were established for an individual whose diet is high in antioxidants/phytochemicals and/or is a vegetarian; an individual whose diet is low in antioxidants/ phytochemicals and/or is a non-vegetarian, or an individual presenting with a medical condition or disorder. The compositions are made up of a variety of nut oils, seed oils, vegetable oils, fruit oils, and other oils, nuts, and seeds. Table 15 presents the ratio ranges of polyunsaturated, monounsaturated, saturated, omega-3, omega-6, and omega-9 fatty acids. Table 16 presents some compositions with the specified ratios of polyunsaturated, monounsaturated, saturated, omega-3, omega-6, and omega-9 fatty acids.

Table 15. Lipid Composition in Ratio Ranges, by Diet Type or Medical Condition

Ratio Ranges by Diet	High Antioxidant/ Phytochemical Diet and/or Vegetarian		Low Antioxidant/ Phytochemical Diet and/ or Non-Vegetarian		Individual with Medical Issues	
	Low	High	Low	High	Low	High
Total Lipids: Monounsaturated Fats	1.50	4.00	1.50	4.00	1.50	4.00
Monounsaturated: Polyunsaturated Fats	1.00	3.00	1.00	3.00	1.00	3.00
Polyunsaturated: Saturated Fats	1.00	3.00	1.00	3.00	1.00	3.00
Monounsaturated: Saturated Fats	1.00	4.00	1.00	4.00	1.00	4.00

O9:O6	1.00	3.00	1.00	3.00	1.00	5.00
O6:O3	4.00	20.00	1.00	8.00	1.00	20.00
O9:O3	5.00	30.00	4.00	10.00	4.00	10.00
O9 % of Total Lipids	22.86	91.43	21.62	86.49	22.86	91.43
O6 % of Total Lipids	12.86	51.43	10.81	43.24	5.71	22.86
O3 % of Total Lipids	0.86	3.43	4.05	16.22	5.71	22.86

Table 16. Lipid Composition Ratios, by Diet Type or Medical Condition

Ratios	High Antioxidant/ Phytochemical Diet and/or Vegetarian	Low Antioxidant/ Phytochemical Diet and/ or Non-Vegetarian	Individual with Medical Issues
Total Lipids: Monounsaturated Fats	2.19	2.31	2.19
Monounsaturated: Polyunsaturated Fats	1.45	1.23	1.45
Polyunsaturated: Saturated Fats	1.38	1.63	1.38
Monounsaturated: Saturated Fats	2.00	2.00	2.00
O9:O6	1.78	2.00	4.00
O6:O3	15.00	2.67	1.00
O9:O3	26.67	5.33	4.00
O9 % of Total Lipids	45.71	43.24	45.71
O6 % of Total Lipids	25.71	21.62	11.43
O3 % of Total Lipids	1.71	8.11	11.43

Example 8. Two-Component Lipid Formulation According to Diet and Medical Condition

[0061] In one example liquid lipid and solid lipid composition parameters were established per diet or medical condition, intended for twice-a-day administration (i.e. 2 component daily formulation). As per Table 17 to Table 20, the parameters of the compositions were established for an individual whose diet is high in antioxidants/phytochemicals and/or is a vegetarian; an individual whose diet is low in antioxidants/phytochemicals and /or is a non-vegetarian, or an individual presenting with a medical condition or disorder. The compositions are made up of a variety of nut oils, seed oils, vegetable oils, fruit oils, and other oils, nuts, and seeds. Table 17 presents the ratios of polyunsaturated, monounsaturated, saturated, omega-3, omega-6, and omega-9 fatty acids for the bar (solid) formulation. Table 18 presents the ratios of polyunsaturated, monounsaturated, saturated, omega-3, omega-6, and omega-9 fatty acids for the liquid formulation. Table 19 presents examples of bar formulation (solid) and Table 20 presents one

liquid composition with the specified ratio ranges of polyunsaturated, monounsaturated, saturated, omega-3, omega-6, and omega-9 fatty acids.

Table 17. Solid Lipid Composition in Ratios, by Diet Type or Medical Condition

2-Component Formulation, Ratios	In Bar Formulation		
Ratios	High Antioxidant/ Phytochemical Diet and/or Vegetarian	Low Antioxidant/ Phytochemical Diet and/ or Non-Vegetarian	Individual with Medical Issues
Total Lipids: Monounsaturated Fats	2.33	2.56	2.40
Monounsaturated: Polyunsaturated Fats	1.50	1.13	1.25
Polyunsaturated: Saturated Fats	1.00	1.33	1.33
Monounsaturated: Saturated Fats	1.50	1.50	1.67
O9:O6	1.33	1.33	1.60
O6:O3	10.00	3.00	2.50
O9:O3	13.33	4.00	4.00
Omega-9 % of Total Lipids	38.10	34.78	33.33
Omega-6 % of Total Lipids	28.57	26.09	20.83
Omega-3 % of Total Lipids	2.86	8.70	8.33

Table 18. Liquid Lipid Composition in Ratios, by Diet Type or Medical Condition

2-Component Formulation, Ratios	In Liquid Formulation		
Ratios	High Antioxidant/ Phytochemical Diet and/or Vegetarian	Low Antioxidant/ Phytochemical Diet and/ or Non-Vegetarian	Individual with Medical Issues
Total Lipids: Monounsaturated Fats	1.87	2.00	2.25
Monounsaturated: Polyunsaturated Fats	1.67	1.36	1.00
Polyunsaturated: Saturated Fats	2.25	2.75	4.00
Monounsaturated: Saturated Fats	3.75	3.75	4.00
O9:O6	1.72	1.75	2.00
O6:O3	41.60	4.00	2.00
O9:O3	71.50	7.00	4.00
Omega-9 % of Total Lipids	51.07	46.67	44.44
Omega-6 % of Total Lipids	29.71	26.67	22.22
Omega-3 % of Total Lipids	0.71	6.67	11.11

Table 19. Solid Lipid Composition in Ratio Ranges, by Diet Type or Medical Condition

	Bar Formulation		
2-Component Formulation, Ratio	High Antioxidant/	Low Antioxidant/	Individual with

Ranges	Phytochemical Diet and/or Vegetarian		Phytochemical Diet and/ or Non-Vegetarian		Medical Issues	
	Low	High	Low	High	Low	High
Total Lipids: Monounsaturated Fats	1.50	4.00	1.50	4.00	1.50	4.00
Monounsaturated: Polyunsaturated Fats	1.00	3.00	1.00	3.00	1.00	3.00
Polyunsaturated: Saturated Fats	1.00	3.00	1.00	3.00	1.00	3.00
Monounsaturated: Saturated Fats	1.00	4.00	1.00	4.00	1.00	4.00
O9:O6	1.00	3.00	1.00	3.00	1.00	5.00
O6:O3	4.00	16.00	1.00	8.00	1.00	16.00
O9:O3	5.00	20.00	4.00	10.00	4.00	10.00
Omega-9 % of Total Lipids	19.05	76.19	17.39	69.57	16.67	66.67
Omega-6 % of Total Lipids	14.29	57.14	13.04	52.17	10.42	41.67
Omega-3 % of Total Lipids	1.43	5.71	4.35	17.39	4.17	16.67

Table 20. Liquid Lipid Composition in Ratio Ranges, by Diet Type or Medical Condition

	Liquid Formulation					
2-Component Formulation, Ratio Ranges	High Antioxidant/ Phytochemical Diet and/or Vegetarian		Low Antioxidant/ Phytochemical Diet and/ or Non-Vegetarian		Individual with Medical Issues	
	Low	High	Low	High	Low	High
Total Lipids: Monounsaturated Fats	1.50	4.00	1.50	4.00	1.50	4.00
Monounsaturated: Polyunsaturated Fats	1.00	3.00	1.00	3.00	1.00	3.00
Polyunsaturated: Saturated Fats	1.00	3.00	1.00	3.00	1.00	4.00
Monounsaturated: Saturated Fats	1.00	4.00	1.00	4.00	1.00	4.00
O9:O6	1.00	3.00	1.00	3.00	1.00	5.00
O6:O3	8.00	45.00	1.00	8.00	1.00	45.00
O9:O3	10.00	75.00	4.00	10.00	4.00	10.00
Omega-9 % of Total Lipids	25.54	90	23.33	93.33	22.22	88.89
Omega-6 % of Total Lipids	14.86	59.43	13.33	53.33	11.11	44.44
Omega-3 % of Total Lipids	0.36	1.43	3.33	13.33	5.56	22.22

Example 9. Special Formulations Based on Diet

[0062] In this example one liquid lipid composition parameters was established and one formulation was prepared, intended for once, twice, or thrice or more a day administration to an individual whose diet is high in antioxidants/phytochemicals and/or is a vegetarian and to an individual who does not favor, or cannot tolerate nuts and seeds. The compositions include a variety of nut oils, seed oils,

vegetable oils, fruit oils, and other oils. Some ranges for a formulation are provided by % by weight (w/w) for each component (representing the % weight for that individual component on a daily basis). The compositions can be administered once or more daily. Some compositions may include two or more of: almond oil (4%-23%), anhydrous butter oil (5%-29%), avocado oil (1%-6%), cashew oil (2%-15%), coconut oil (0%-2%), corn oil (3%-19%), fish oil (0%-5%), flaxseed oil (0%-5%), mustard oil (0%-5%), olive oil (3%-17%), palm oil (0%-5%), peanut oil (5%-30%), pistachio oil (1%-7%), pumpkin seed oil (1%-8%), safflower oil (high oleic) (1% - 5%), sesame seed oil(0% - 5%), soybean lecithin (0%-5%), soybean oil (1%-7%), sunflower oil (high oleic) (2% -14%), sunflower oil (regular) (0%-5%), and/or walnut oil (3%-15%).

[0063] Another set of parameters for one liquid lipid composition was established, intended for once, twice, or thrice a day administration to an individual who does not favor, or cannot tolerate nuts and seeds. The compositions included a variety of nut oils, seed oils, vegetable oils, fruit oils, and other oils. Some ranges for a formulation are provided by % by weight (w/w) for each component (representing the % weight for that individual component on a daily basis). The ranges can accommodate vegetarian/high-antioxidant/high-phytochemical user and omnivore/low-antioxidant/low-phytochemical user or a seafood user, in different combinations. The compositions can be administered once or more daily. Some compositions may include two or more of: almond oil (2%-36%), anhydrous butter oil (2%-36%), coconut oil (0%-8%), corn oil (1%-24%), flaxseed oil (0%-8%), mustard oil (0%-8%), olive oil (2%-36), palm oil (0%-2%), peanut oil (4%-72%), pumpkin seeds oil (1%-24%), safflower oil (high oleic) (2% - 60%), soybean lecithin (0%-4%), sunflower oil (high oleic) (4% -72%), and/or walnut oil (2%-36%).

Example 10. Daily Formulations

[0064] Liquid lipid and solid lipid composition parameters were established for a twice-daily administration (i.e. 2-component daily formulations). The compositions were made up of a variety of nut oils, seed oils, vegetable oils, fruit oils, and other oils. The ranges for each component of the liquid and solid formulations are presented for each of the solid and liquid formulations. The solid formulation includes two or more of by % weight of total composition: almonds (10% - 25%), cashews (7% -15%) coconut shredded (1% -4%), flaxseed (0% -1%), olives (15%

-25%), peanuts (4% -15%), pistachios (2% -9%), pumpkin seeds (2% -12%), sesame (0% -10%), soybeans (8% -20%), sunflower seeds (1% -4%), and/or walnuts (5% -15%). The liquid formulation includes two or more of by % weight of total composition: avocado oil (3% -14%), corn oil (15% -30%), mustard oil (0% -2%), olive oil (10% -22%), palm oil (0% -2%), peanut oil (15% -35%), safflower oil (high oleic)(5% -15%), soybean lecithin (0% -2%), sunflower oil (high oleic)(10% -25%), and/or anhydrous butter oil (5% -15%).

[0065] Some parameters were also established for one or more daily administration (e.g., 1, 2 or 3 component daily formulation). The compositions were made up of a variety of nuts, seeds, nut oils, seed oils, vegetable oils, fruit oils, and other oils. The ranges for each component of the formulations are presented for each of the solid and liquid components. The formulation can include two or more of by % weight of total composition: peanuts or peanut oil (4%-35%), almonds or almond oil (2%-25%), olives or olive oil(3%-45%), legumes or grains (15%-45%), cashews or cashew oil (10%-40%), pistachios or pistachio oil (5%-25%), pumpkin seeds or pumpkin seed oil (4%-25%), sunflower seeds or sunflower seed oil (2%-30%), sesame seeds or sesame seed oil (0%-20%), walnuts or walnut oil (5%-25%), flaxseed or flaxseed oil (0%-10%), anhydrous butter oil or milk product including cheese (5%-45%), coconut meat or coconut oil (2%-8%), corn oil (3%-20%), avocado oil (3%-8%), safflower oil (2%-20%), mustard oil (0%-8%), palm oil (0%-8%), and/or soybean lecithin (0%-2%).

Example 11. A Case Study on Menopause, Aging, and Musculoskeletal Disorders

[0066] A 47-year old female presented with menopause-related hot flushes. The subject's diet was supplemented with a combination of vegetable oils, seed oils, nuts and seeds for a period of 6 weeks. The subject was provided with the twice-daily administration formulation in Example 10. By optimizing omega-6 and omega-3 fatty acids and ratios in the context of the compositions, it was observed that there was an adaptation period over which the intensity of hot flushes gradually diminished. Other symptoms reduced were: night sweats, loss of libido, vaginal dryness, fatigue, hair loss, sensitivity to hot and cold, sleep disorders, difficulty concentrating, memory lapses, weight gain, bloating, mood swings, depression, anxiety, irritability, breast tenderness, migraines, aching joints, burning tongue, the feeling of electric shocks, digestive problems, gum problems, muscle tensions, itchy skin, and tingling in the extremities, as reported by the

subject. During the 6-week course of treatment, the subject improved her posture, which is indicative of greater muscle mass, joint and/or tendon strength and flexibility, and bone density. The effect on osteoporosis can be tested by continuing the treatment with the supplement of oils, nuts, and seeds over a longer period of time and measuring bone density, using standard methods, before, during, and after treatment.

[0067] It is likely that beneficial effects of treatment on the menopause-related symptoms was due to achieving steady sex-hormone-like benefit from omega-6 and omega-3 fatty acid supplementation and optimization in context of antioxidants and phytochemicals. The amount of dietary fat, its composition, and the period during which the nutrient is fed to animals is known to affect the secretion and metabolism of androgens and endogenous steroids, and the presentation of sex hormone receptor on the cell surface. Estrogens and polyunsaturated fatty acids are also believed to have similar actions. In addition to amount and composition, relatively steady dosages may also be important to reduce hormone fluctuations. Das UN. Estrogen, statins, and polyunsaturated fatty acids: similarities in their actions and benefits-is there a common link? Nutrition. 2002 Feb;18(2):178-88. McVey MJ, Cooke GM, Curran IH, Chan HM, Kubow S, Lok E, Mehta R. Epub 2007 Sep 11. Effects of dietary fats and proteins on rat testicular steroidogenic enzymes and serum testosterone levels. Food Chem Toxicol. 2008 Jan;46(1):259-69. Gromadzka-Ostrowska J. Effects of dietary fat on androgen secretion and metabolism. Reprod Biol. 2006;6 Suppl 2:13-20.

[0068] Nutrients from the total diet (natural sources) including the lipid composition administered were as follows in Table 21.

Table 21. The Subject's Daily Nutrients

Nutrient	Weight	Nutrient	Weight
Protein g	60-100	Cystine g	1-2.5
Carbohydrate g	225-325	Glutamic acid g	12-14
Total Lipids g	50-65	Glycine	2-4
Calories	1700-1900	Histidine g	1-3
Cholestrol mg	150-300	Isoleucine g	2-4.5
Fiber g	30-45	Leucine g	4.5-7.5
Alpha Carotene mcg	3000-4000	Lysine g	4-5.5
Beta Carotene mcg	10000-14000	Methionine g	1-2.5
Beta Cryptoxanthin mcg	600-850	Phenylalanine g	2.5-4.5
Betaine mg	20-50	Proline g	4-6
Choline mg	150-250	Serine g	2.5-5.5
Folate mcg	500-800	Threonine g	2-4

Nutrient	Weight	Nutrient	Weight
Lycopene mcg	1600-1900	Tryptophan g	0.5-2
Lutein Zeaxanthin mcg	10000-14000	Tyrosine g	2-4
Niacin mg	15-20	Valine g	3-5
Pantothenic Acid mg	8-14	Total Fat g	50-65
Retinol mcg	300-400	Monounsaturated g	18-26
Riboflavin mg	2-3	Polyunsaturated g	12-18
Thiamin mg	1.5-2.5	Saturated g	12-17
Vitamin E Tocopherol Beta mg	0.1-0.5	Butyric acid 4:0 g	0.2-.75
Vitamin E Tocopherol Delta mg	0.1-0.5	Caproic acid 6:0 g	0.1-0.5
Vitamin E Tocopherol Gamma mg	2.0-4.0	Caprylic acid 8:0 g	0.1-0.5
Vitamin E Tocopherol Alpha mg	10-15	Caprice acid 10:0 g	0.2-0.6
Vitamin A IU	20000-30000	Lauric acid 12:0 g	0.4-0.75
Vitamin A RAE	1500-1900	Myristic 14:0 g	1-3.0
Vitamin B6 mg	1.5-2.5	Palmitic 16:0 g	3.0-7.0
Vitamin B12 mcg	2-5	Palmitoleic 16:1 g	0.25-1.5
Vitamin C mg	250-400	Stearic 18:0 g	1.5-3.0
Vitamin D IU	200-400	Oleic 18:1 g	16-22
Vitamin K mcg	300-550	Linoleic 18:2 g	11-14
Calcium mg	1200-1500	Alpha-linolenic 18:3 g	0.8-1.5
Copper mg	2-3	Arachidic 20:0 g	0.1-1.0
Iron mg	14-18	Gadoleic (Eicosenoic) 20:1 g	0.1-.4
Magnesium mg	400-700	Arachidonic 20:4 g	0.01-0.5
Manganese mg	6-8	Eicosapentaenoic 20:5 g	0-0.5
Phosphorous mg	1600-1900	Erucic 22:1 g	0-.0.3
Potassium mg	3800-5500	Docosapentaenoic 22:5 g	0-0.5
Selenium mcg	65-80	Docosahexaenoic 22:6 g	0.01-0.2
Sodium mg	2000-2500	Phytosterols mg	90-150
Zinc mg	10-14	Campesterol mg	0.8-1.5
Alanine g	2.5-4.5	Sitosterol mg	15-30
Arginine g	3-4.5	Stigmasterol mg	0.3-1.5
Aspartic acid g	6-8		

Example 12. A Case Study on Hypercholesterolemia, Cardiovascular Disease

[0069] The host subject experienced hypercholesterolemia on a vegetarian diet low in fat, mostly olive oil (75% monounsaturated fat), a daily fish oil supplement of 1 gram, and a daily total essential fatty acids (EFA) supplement of 1 gram. As part of the treatment, the fish oil and EFA supplements were discontinued. The subject was then administered a daily lipid composition supplement containing 11 grams of omega-6 and 1.2 grams of omega-3 fatty acids, made up primarily from a combination of vegetable oils, and nuts and seeds. Administration of the lipid composition resulted in a reduction of LDL from 160mg to 120mg. Very low levels of blood pressure were observed, 90/55 mmHg, when omega-3 were increased to 1.8 grams; blood pressure levels normalized at 105/70 mmHg at 11 grams of omega-6 and 1.2 grams of omega-3 fatty acids. When omega-3 were

reduced from 1.8 grams to 1.2 grams per day, the subject experienced an irregular heartbeat, which subsided over a period of 2-3 weeks. However, when omega-3 were further reduced to 0.5 grams per day, it resulted in an ongoing arrhythmia.

[0070] This case study demonstrated that supplementation with vegetable oils, nuts, and seeds, wherein the omega-6 to omega-3 fatty acids ratio was about 9:1 may result in a significant decrease in LDL cholesterol blood levels (dyslipidemia which is associated with atherosclerosis). This case study also demonstrated that the lipid compositions and ratios described herein may be useful in moderating blood pressure and arrhythmia.

[0071] In another human subject, intense muscle spasms arising from the left thoracic cavity/wall were observed subsequent to a meal high in omega-6 fatty acids, whereas the subject's typical diet included primarily monounsaturated fatty acids and very small amounts of saturated fatty acids. It is hypothesized, that sudden increase in omega-6, when the body is chronically deficient may be harmful.

[0072] Polyunsaturated fatty acids (omega-3 and omega-6, particularly gamma-linolenic acid) have often been recommended to reduce coronary heart disease along with recommendations to reduce saturated fatty acids. But all saturated fats do not have the same effect on cholesterol synthesis in the liver. Saturated fats of chain-length 12, 14 and 16 (lauric acid, myristic acid and palmitic acid) have been shown to elevate blood cholesterol. Stearic acid (18-carbon, saturated) has been shown to lower cholesterol by 21%--even more than oleic acid (18-carbon, monounsaturated), which lowers LDL by 15%. Polyunsaturated fatty acids increase cell membrane fluidity and therefore tissue flexibility, including that of the arteries. It has been suggested that reduced activity of Delta6 and Delta5 desaturases, enzymes that metabolize essential fatty acids may be a factor in the initiation and progression of atherosclerosis. Das UN. A defect in the activity of Delta6 and Delta5 desaturases may be a factor in the initiation and progression of atherosclerosis. Prostaglandins Leukot Essent Fatty Acids. 2007 May;76(5):251-68. Epub 2007 Apr 26. However, certain phytochemicals have been shown to inhibit the enzymatic activity. Fujiyama-Fujiwara Y, Umeda R, Igarashi O. Effects of sesamin and curcumin on delta 5-desaturation and chain elongation of polyunsaturated fatty acid metabolism in primary cultured rat hepatocytes. J Nutr Sci Vitaminol (Tokyo). 1992 Aug;38(4):353-63. This suggests that dietary phytochemicals may change the requirement/metabolism of essential fatty acids.

The reduction in formation of long-chain omega-6 Arachidonic acid may be desirable to reduce its excessive activity, but beyond a point it may lead to deficiency of a critical cell-membrane component and its metabolites.

Example 13. A Case Study on Mood Swing, Mental Function

[0073] The subject host was placed on a trial of varying ratios of omega-6 and omega-3 fatty acids using various oils and nut combinations. Each time omega-3 were reduced or omega-6 were increased the subject became depressed and was given to crying at the slightest provocation. When omega-3 were increased, it elevated the subject's mood, immediately noticeable. However, within certain ranges of omega-6 and omega-3, the effect was self-adjusting, e.g., over a period of 3-6 weeks the moods normalized. It was also observed that within that range of omega-6 and omega-3 fatty acids, over a period of 3-6 weeks the subject in fact was more grounded at higher levels of omega-6; and was euphoric at higher levels of omega-3. Omega-3 increase enhanced cognitive function, which was immediately noticeable. Omega-3 reduction caused confusion, dyslexia, and a decline in cognitive function but these symptoms subsided with time, again within certain omega-6 and omega-3 fatty acids ranges. The subject also displayed greater attention span and concentration after omega-6 and omega-3 were optimized over a period of 3-6 weeks, with greater reading speeds and comprehension. Thus, the subject performed better at a lower level of omega-3 fatty acids, which suggests that an adaptation mechanism was activated to compensate for the required level of omega-6 metabolites at higher levels of dietary omega-3 fatty acids. There may be a similar adaptation mechanism for required level of omega-3 metabolites, when inadequately supplied from diet. The cumulative effects of such adaptations could pose a threat to the individual in the long run.

[0074] Manipulation of dietary fats can alter the fatty acid composition of brain-cell membranes, with effects on thought processing and behavior. Polyunsaturated fatty acids could be associated at different levels in brain functions through their role in the membrane fluidity which influences diverse steps of neurotransmission and through their function as precursors of pro-inflammatory cytokines and eicosanoids disturbing neurotransmission. Though harmful in excess, cytokines and lipid peroxidation products may exert beneficial effects at low levels. Some studies have found lessened lipid per-oxidation in Attention-Deficit Hyperactivity

Disorder among children, suggesting the need to balance lipids with respect to antioxidants. Spahis S et al. "Lipid profile, fatty acid composition and pro- and anti-oxidant status in pediatric patients with attention-deficit/hyperactivity disorder." Prostaglandins Leukot Essent Fatty Acids. 2008 Jul-Aug;79(1-2):47-53. Epub 2008 Aug 30.

Example 14. Case Studies on Neural Disorders

1. Progressive Supra-nuclear Palsy

[0075] The subject host was a 50-year old woman whose symptoms included dental sensitivity, deteriorating muscle mass, occasional breathing difficulty, easy bruising, mild arrhythmia, and difficult bowel movement. A dentist, as a solution to her sensitive teeth, had extracted and replaced her teeth with dentures at 50. Each of her other symptoms was treated as a stand-alone symptom and treated with non-lipid medications. At 60 she developed loss of balance, diplopia (double vision), and slurry speech. Eventually when she started having bone-shattering falls, she was diagnosed with Progressive Supra-nuclear Palsy (PSP), a neurological disease mainly characterized by loss of neural tissue in the brainstem. The subject then lost ambulation and speech, and developed dysphagia. She passed away at 67 from pneumonia.

[0076] The woman had had four healthy deliveries, a healthy life until 50, and had no incidence of neural disease in her family. Closer examination of changes in her life around 50 revealed that around that time the fats in her diet had been significantly cut back because of the prevalent doctrine in the 1980s that fats cause heart-disease, and that all fats are deleterious. Both of the woman's parents in their early 70s, and a brother at 48, had died of myocardial infarctions. Hence, the fat reduction was a precautionary measure to avoid cardiac disease, which was then believed to have a strong genetic component. However, it is hypothesized in the present disclosure that the fats were cut to a point where she became severely deficient in both omega-6, and omega-3 fatty acids. The woman was a postmenopausal vegetarian with high antioxidant and phytochemicals intake, and the little fat that was in her diet was either saturated fat (less than 20% of total fat) or monounsaturated fat (70-90% of total fat), mostly olive oil following the then doctrine that held olive oil above all others. Olive oil is 75% monounsaturated oil and rich in polyphenols. Since all fatty acids compete in the metabolic pathway and antioxidants and phytochemicals increase the requirement for omega-6, in her

case the deficiency of omega-6 acid appears to be the bigger culprit. The deficiency of omega-6 is also evident from her early symptoms: muscle mass requires a balance of omega-6 and omega-3, lack of omega-6-derivative leukotrienes may lead to asthma-like breathing issues (conversely excessive leukotrienes can also lead to asthma like symptoms), deficiency of omega-3 has been linked with arrhythmia, and deficiency of omega-6 derived thromboxanes may lead to easy bruising, and lack of omega-6 derived prostaglandins may impede smooth muscle activity and therefore the bowel movement. The fact that she was post-menopausal made the requirement of omega-6 and omega-3 more critical, since estrogen and androgens, as hypothesized in the present disclosure, have similar actions and benefits as polyunsaturated fats. When the reproductive hormones decline, the body may increasingly depend on omega-6 and omega-3 fatty acids and their metabolites for the physiological functions.

[0077] It is an embodiment of the present disclosure, that deficiency of Linoleic acid (LA) metabolite Arachidonic acid (AA) and Alpha-linolenic acid (ALA) metabolite Docosahexaenoic acid (DHA), that are so abundantly present in neural tissue, particularly the membranes of neural synapses, may have caused the neurodegeneration. Neuroinflammation is a host defense mechanism associated with neutralization of an insult and restoration of normal structure and function of brain, and is characteristic of all major neural diseases. The dietary deficiency of LA and ALA, and the resulting unfavorable tissue ratio of AA to DHA might have affected the neurodegeneration associated with acute neural trauma and neurodegenerative disease.

[0078] It is important to note that not all omega-6 or omega-3 fatty acids deficiencies or imbalance lead to PSP. It simply creates a distress in the body; the disease developed depends on rest of the body chemistry. In the Western world omega-3 fatty acids have received much attention because the populace's consumption was highly skewed towards omega-6 and that with inadequate antioxidant and phytochemical intake. Requirement of omega-3 may be very small, and may increase only with the increase in omega-6. Disclosed herein are methods and compositions to balance omega-3 and omega-6 fatty acids, in light of demographic factors, and for their steady delivery.

2. Amyotrophic Lateral Sclerosis

[0079] The subject was a vegetarian woman in her mid-30s, on a low-fat diet using primarily olive oil and nuts. She had developed Amyotrophic Lateral Sclerosis (ALS)-like symptoms: muscle weakness in hands, arms, legs, and the muscles of speech, twitching and cramping of muscles, shortness of breath, and difficulty in swallowing. The left side of her body was affected more than the right side. Upon administration of a lipid composition and changes in diet that increased omega-6 fatty acids to about 12 grams, her symptoms disappeared and the muscle tone improved, better than before the onset of symptoms. It is hypothesized that in this instance, the amount of omega-3 relative to omega-6 in the tissue had exceeded the ratio tolerated by the body. Since the vegetarian diet and nuts contributed plenty of antioxidants and phytochemicals, the subject might have become deficient in omega-6 fatty acids and the required metabolites, despite moderate levels of dietary omega-3 fatty acids.

[0080] The initial symptoms of ALS can be quite varied in different people. One person may experience tripping over carpet edges, another person may have trouble lifting and a third person's early symptom may be slurred speech. In a small number of people, ALS is known to remit or halt its progression, though there is no scientific understanding as to how and why this happens. It is hypothesized herein that it has to do with inadvertent change in omega-6 and omega-3 fatty acids consumption. Most of us fall into certain food patterns based on likes and dislikes, habits inherited from family, accessibility of certain foods, cooking habits, and the foods that happen to be in vogue. But, there is always that change in life, a dinner party at a friend's, food gift from a well-wisher, or a vacation to a remote locale, or a new oil that one takes a liking to, which brings about change in diet. All it takes is a handful of nuts, or a spoonful of high-omega-6 and/or omega-3 oil to tip the balance, even if temporarily. However little, it does register in the body.

[0081] Subsequent to the experimental adjustment of omega-6 and omega-3 fatty acid levels in other host subjects through the disclosed compositions, improvement in motor coordination, handwriting, balance, and body's ability to follow a rhythm, in dance steps for example, were observed.

Example 15. Case Studies on Musculoskeletal Disorders

1. Muscular Performance

[0082] In a host subject , many musculoskeletal issues appeared and disappeared during the course of omega-6 and omega-3 fatty acids therapy through the administration of the lipid compositions. Increases in omega-3 beyond 0.5g, in a vegetarian host with omega-6 at 10-11 grams, yielded better muscular performance, lesser joint pain, lesser joint crackling sounds, and better spatial task performance. But a point of diminishing marginal returns was reached at about 1.2 grams of omega-3. Increases of omega-3 beyond 1.2 grams resulted in weaker muscle tone, posture, and exercise endurance. When the omega-3 was gradually brought back to 1.2 grams, the subject experienced leg cramps, lower back pain, burning sensation in the scalp, buckling of knee joints, and joint pains in knees and shoulders. Over a period of 3-6 weeks these symptoms subsided.

2. Gout

[0083] Another host subject, had developed Gout, a joint disorder, on a low-fat diet, primarily olive oil, and nuts. The symptoms disappeared upon increase of omega-6 in the diet.

3. Myofascial Pains and Thoracic Outlet Syndrome

[0084] In a 35-year old vegetarian female, on a low-fat diet using olive oil as the main fat in the diet, the development of episodes of acute myofascial pains were observed. The subject experienced severe muscle tightness in several areas of the body, neck shoulders, para-spinal muscles, thighs, hands, and arms.

[0085] The host was diagnosed with Myofascial Pain Syndrome (MFS) and Thoracic Outlet Syndrome (TOS). TOS consists of a group of distinct disorders that affect the nerves in the brachial plexus (nerves that pass into the arms from the neck) and the subclavian artery and vein blood vessels between the base of the neck and axilla (armpit). For the most part, these disorders are produced by compression of the components of the brachial plexus (the large cluster of nerves that pass from the neck to the arm), the subclavian artery, or the subclavian vein. Neurogenic form of TOS accounts for 95-98% of all cases of TOS, hence neural disease was suspected. The host subject went through numerous examinations including: MRIs of the entire CNS, X-rays, blood work, drug therapies, massage therapies, and chiropractic treatment. The symptoms would go away and then reappear a few months or a year later. After omega-6 and omega-3 in the subject's diet were

optimized by administration of the disclosed lipid compositions, the episodes of TOS and myofascial pains subsided. It is hypothesized herein that these episodes were the result of the body being severely deficient in omega-6 and omega-3 fatty acids. Each time there was an inadvertent increase in omega-6 and omega-3 fatty acids, more particularly omega-6 fatty acids, which can occur by any incidental changes in diet, there may have been a sudden surge in prostaglandins, thromboxanes, and leukotrienes, and excitability of neural and muscle cells, resulting in severe muscular tightening. Other mechanisms related to the lipids may be involved that are not yet understood.

[0086] Fatty acids' relationship with musculoskeletal disorders is very intricate. There are many studies demonstrating that arachidonic acid and other polyunsaturated fatty acids modulate the function of voltage gated calcium, sodium, and potassium channels, primarily in neural and muscle cells impacting the excitability of the cells. Boland LM, Drzewiecki MM. Polyunsaturated Fatty Acid modulation of voltage-gated ion channels. Cell Biochem Biophys. 2008;52(2):59-84. Epub 2008 Oct 2. In some studies changes in muscle fiber type have been observed with changes in amount and type of fatty acids. de Wilde J, Mohren R, van den Berg S, Boekschoten M, Dijk KW, de Groot P, Müller M, Mariman E, Smit E. Short-term high fat-feeding results in morphological and metabolic adaptations in the skeletal muscle of C57BL/6J mice. Physiol Genomics. 2008 Feb 19;32(3):360-9. Epub 2007 Nov 27. On the skeletal side, bone mass is governed by balanced action of osteoblasts (bone forming cells) and osteoclast (bone resorbing cells). There is increasing evidence that various long-chain polyunsaturated fatty acids and their metabolites affect calcium balance, osteoblastogenesis, osteoclastogenesis, and osteoblast and osteoclast function. Poulsen RC, Moughan PJ, Kruger MC. Long-chain polyunsaturated fatty acids and the regulation of bone metabolism. Exp Biol Med (Maywood). 2007 Nov;232(10):1275-88. Rahman MM, Bhattacharya A, Fernandes G. Docosahexaenoic acid is more potent inhibitor of osteoclast differentiation in RAW 264.7 cells than eicosapentaenoic acid. J Cell Physiol. 2008 Jan;214(1):201-9.

Example 16. A Case Study on Thyroid Disturbances

[0087] In a host subject, symptoms of thyroid disturbance with a decrease in omega-3 fatty acids, fatigue and weakness, cold intolerance, hair loss, cold hands and feet, weight gain, insomnia, constipation, depression, poor memory, forgetfulness, and

nervousness were observed, which were self-adjusting within optimal fatty acids ranges.

Example 17. A Case Study on Weight Gain, Obesity

[0088] In a vegetarian host subject it was discovered that there was a band of optimal quantity and ratio of omega-6 and omega-3 fatty acids, beyond which the subject gained weight. At omega-6 of 11 grams and omega-3 of 2 grams, the subject was at 134 lbs. Upon gradual reduction of omega-3 to 1.2 grams, the subject initially gained 6 lbs., and then after 6 weeks, lost 12 lbs. for an ending weight of 128 lbs. Obesity often has been linked to slow metabolism. In turn, metabolic rate has been linked to cell-membrane composition. Hulbert AJ. Membrane fatty acids as pacemakers of animal metabolism. Lipids. 2007 Sep;42(9):811-9. Epub 2007 Apr 27. High polyunsaturated membrane composition may be linked with fast membrane associated processes. Membrane composition influences all aspects of the energy balance equation: electrolyte gradient balance, neuropeptide regulation, gene regulation and glucose regulation.

Example 18. A Case Study on Diabetes

[0089] Varying quantities and ratios of omega-6 and omega-3 fatty acids were administered to otherwise healthy subjects to see if very early symptoms of diabetes could be induced. High blood sugar, excessive urine production, excessive thirst and increased fluid intake, blurred vision, unexplained weight gain and lethargy were induced by certain ratios and amounts of omega-6 and omega-3 fatty acids within the context of disclosed compositions. These simulated symptoms with very high levels of omega-3 may also be reversed by reducing the dosage. In one instance, insulin resistance may be associated with low levels of omega-6 fatty acids. Summers LK, Fielding BA, Bradshaw HA, Ilic V, Beysen C, Clark ML, Moore NR, Frayn KN. Substituting dietary saturated fat with polyunsaturated fat changes abdominal fat distribution and improves insulin sensitivity. Diabetologia. 2002 Mar;45(3):369-77.

Example 19. A Case Study on Digestive System Disorders

[0090] In the host subject, incidences of acid reflux disease, irritable bowels, indigestion, and dyspepsia were observed. Each time omega-6 fatty acids were increased or omega-3 fatty acids were decreased the following symptoms appeared: stomach pain, bloating, heartburn, nausea (upset stomach), and burping; but they all disappeared as the body adjusted to increased omega-6. Omega-6 were tested up

to 11 grams. It is hypothesized that beyond that point in the particular host the symptoms would persist. Increasing omega-3 beyond 2 grams caused tight dark pellet-like stools. In the optimal omega-6 and omega-3 balance, bile production was optimal as determined by the yellowish brown color of the stools. It was also observed that mucus production in the alimentary canal was optimal with the proper omega-6 and omega-3 quantities and ratio, using mucus production in the oral cavity as an indicator. Halitosis was also observed with 2 grams of omega-3, and got worse when omega-3 were reduced, and then normalized over a period of 3-6 weeks. Arachidonic acid plays a pivotal role in protection and integrity of the intestinal mucosa. Excessive omega-3 can displace arachidonic acid leading to gastro-intestinal mucosal damage.

Example 20. A Case Study on Ovulation, Reproductive Disorders

[0091] In a host subject, a 35-year old female, cessation of ovulation (as indicated by watery pale menstrual cycles), intense ovulation-related pains and anovulatry menstruation at extremely low omega-6 fatty acids in diet were observed; olive oil being the main fat source. It is hypothesized herein that this was due to deficiency of omega-6 derived prostaglandins, which aid ovulation. The same phenomenon was observed when the subject was put on Advil, which blocks cyclooxygenase activity and therefore the prostaglandin synthesis.

[0092] Dietary fatty acids are intricately linked with reproduction from menstruation, to fertilization, to gestation-related complications such as diabetes, to development of the fetus, to pre-term delivery, to post-natal health of the mother and the child.

Example 21. Case Studies on Aging, Tissue Repair

[0093] In host subjects, symptoms of aging were modulated by balancing and optimizing omega-6 and omega-3 fatty acids via the disclosed compositions, including muscle mass restoration, stabilizing sleep, increasing mental sharpness, increasing energy and vigor, improved skin, reduction in hair loss, improving bowel function, improving libido and sexual function, and weight management. The management of frequent urination with the ideal balance of omega-6 and omega-3 through the disclosed compositions was also observed. It is hypothesized that this is due to combined effect of management of omega-6 and omega-3 fatty acids in tissue, related eicosanoids, and their effect on physiological functions, and due to the sex-hormone-like effect of these lipids, and due to their effect on the

optimization of sex hormone production; further aided by antioxidants and phytochemicals in the compositions.

[0094] It has been suggested that lipid per-oxidation, though required at moderate levels, may be a significant factor in aging. Oxidative stress may also damage other important biological molecules such as, nucleic acids and proteins. Hulbert AJ. "Life and Death: Metabolic Rate, Membrane Composition, and Life Span of Animals" Physiol Rev. 2007 Oct;87(4):1175-213. Although membrane fluidity may be associated with youth, introduction of more and more double bonds beyond the first 2-3 may not yield additional fluidity. Furthermore, lipid per-oxidation may be associated with reduced membrane fluidity. The disclosed compositions make effective use of natural antioxidants and phytochemicals to manage per-oxidation and retain membrane fluidity, while avoiding excessive omega-3 delivery; omega-3 family of fatty acids with 3-6 double bonds, are the fatty acids most susceptible to per-oxidation. The fibroblast is a type of cell that synthesizes the extra-cellular matrix and collagen, the structural framework for animal tissues. Proper fibroblast function is essential for optimal tissue repair and regeneration. Polyunsaturated fatty acids, antioxidants, and sterols may create a favorable fibroblast plasma membrane environment, and are believed to play a role in electrochemical gradient across the bilayer-lipid membrane. Schroeder F, Kier AB, Sweet WD. Role of polyunsaturated fatty acids and lipid peroxidation in LM fibroblast plasma membrane transbilayer structure. Arch Biochem Biophys. 1990 Jan;276(1):55-64. Haines TH. Do sterols reduce proton and sodium leaks through lipid bilayers? Prog Lipid Res. 2001 Jul;40(4):299-324. The present disclosure also provides compositions and methods for tissue repair and/or regeneration by induction and maintenance of endogenous stem cell proliferation and/or differentiation including by providing the environment for the stem cells to proliferate and/or differentiate. Intestinal cells and bone marrow cells offer examples of adult stem cells for their abundance and their role in the continuous, lifelong, physiological replenishment of circulating cells. . The disclosed compositions and methods also restrict calories, which may extend life by restricting oxidative stress and yielding lower membrane unsaturation index.

Example 22. A Case Study on Pulmonary Disorders

[0095] In a host subject, an increase of omega-6 fatty acids or a decrease of omega-3 fatty acids was associated with breathing difficulty, nasal congestion, earache,

sneezing, and excess mucus. But within the optimal ranges of omega-6 and omega-3, it was self-adjusting over a period of time. A low-fat diet, primarily monounsaturated fats, a total essential fatty acid (EFA) supplement of 1 gram, and a fish oil supplement caused dyspnea in the host subject. The dyspnea disappeared when supplemented with 10-11 grams of omega-6 fatty acids. It is hypothesized that the EFA supplement was not adequately producing the required leukotrienes. Omega-6 and omega-3-derived leukotrienes are very important agents in lung function. They help bring the needed cells to the tissue, and they increase vascular permeability. In excess they can cause airflow obstruction, increased secretion and accumulation of mucus, bronchial constriction, and inflammation. The adjustment period indicates that sudden and wide changes in EFA may upset the immune system, creating a period of heightened vulnerability to pathogens. Further studies may find a link with susceptibility to common colds and influenza with sudden and wide changes in omega-6 and omega-3 fatty acids.

Example 23. A Case Study on Ophthalmologic Disorders

[0096] In a host subject, dry eye and pressure-like ache in the eye was observed upon reduction of omega-3 and an increase of omega-6 fatty acids. When levels of omega-6 and omega-3 were kept within suitable ranges by demographic type, the symptoms disappeared over time. It was also observed that drusen, excessive eye mucus that often gathers in the corners of the eyes, could be gotten rid of with proper omega-6 and omega-3 balance in context of the compositions of the present disclosure. However, when omega-6 or omega-3 were excessively increased the dry eye syndrome persisted. Excessive omega-3 also resulted in very thin blood, possibly due to thromboxanes action reduction, and therefore caused blood-shot eyes.

[0097] Docosahexaenoic acid (omega-3) is an important component of retinal photoreceptors and brain synaptic membranes, and arachidonic acid (omega-6) is an important component of vascular endothelial cells. Moreover, since omega-6 also has a role in vascular blood pressure, both omega-6 and omega-3 are critical to optic health. Although omega-3 fatty acids, and formulations of vitamins C, E, beta-carotene, and zinc have been shown to be preventative in progression of age-related macular degeneration (AMD); increased intakes of lutein/ xeaxanthin and omega-3 fatty acids are associated with progression of AMD, whereas moderate intakes lutein/ xeaxanthin and omega-3 are associated with greater optic health;

suggesting the role of phytochemicals, and the importance of dosage. Robman L, Vu H, Hodge A, Tikellis G, Dimitrov P, McCarty C, Guymer R. Dietary lutein, zeaxanthin, and fats and the progression of age-related macular degeneration. Can J Ophthalmol. 2007 Oct;42(5):720-6.

Example 24. Case Studies on Dermatological Disorders

[0098] Host subjects demonstrated large amounts of omega-3 fatty acids in the diet increased the size of the skin pores, whereas large amounts of omega-6 fatty acids in the diet made skin dry. Balancing the two gave the best results. Fine lines may be reduced using the correct balance in context of the disclosed compositions. Omega-3 reductions at times, may be associated with the appearance of a rash around the neck area. It is hypothesized that a sudden increase in cytokine activity from an increase in omega-6 metabolism produced the skin rash. Brittle nails and foot corns and calluses may disappear with the proper balance of fatty acids through the disclosed compositions. Sloughing of skin, as in dead cells coming to the surface after omega-3 fatty acids reduction, was also observed.

[0099] Skin displays highly active metabolism of polyunsaturated fatty acids. Deficiency of dietary omega-6, linoleic acid has been shown to result in scaly dermatoses and disruption of the skin barrier system, Linoleic acid intake combined with high intakes of vitamin C are associated with better skin-aging appearance. Dietary hempseed oil has been shown to cause significant changes in plasma fatty acid profiles and improved clinical symptoms of atopic dermatitis, which may be due to the abundant supply of both omega-6 and omega-3 fatty acids in hempseed oil. Ziboh VA. Prostaglandins, leukotrienes, and hydroxy fatty acids in epidermis. Semin Dermatol. 1992 Jun;11(2):114-20. Ziboh VA, Cho Y, Mani I, Xi S. Biological significance of essential fatty acids/ prostanoids/ lipoxygenase-derived monohydroxy fatty acids in the skin. Arch Pharm Res. 2002 Dec;25(6):747-58. Cosgrove MC, Franco OH, Granger SP, Murray PG, Mayes AE. Dietary nutrient intakes and skin-aging appearance among middle-aged American women. Am J Clin Nutr. 2008 Aug;88(2):480.

Example 25. Case Studies on Sleep Disorders

[00100] It was observed that use of optimized levels of omega-6 and omega-3 fatty acids through the disclosed lipid compositions by demographic type, more restful sleep and normalization of sleep and wake hours in host subjects may be achieved. In fact, a more restful sleep with a sleep time reduction to 7 hours from 8 in one

host subject, over time was observed. Restless leg syndrome may also be relieved in host subjects. Each time omega-6 and omega-3 amounts were changed the host went through an adjustment period. Omega-3 was more sleep inducing, and increased the total sleep time; omega-6 though was sleep-inducing at first caused a strong rebound of awakening few hours later, to the point of causing temporary insomnia, but over two weeks sleep patterns normalized. It is hypothesized this is because of the effect of omega-6 and omega-3 fatty acids on thyroid function and the effect of thyroid function on sleep, among other mechanisms, such as PGD2 action.

[00101] Omega-6 metabolite PGD2 is believed to be a strong sleep-inducing agent, with a strong rebound of wakefulness reaching insomnia, and a dose-dependent bell-shaped response curve. In other studies omega-3-deficient diet has been shown to lessen the pineal melatonin rhythm, weaken the endogenous functioning of the circadian clock, and to play a role in nocturnal sleep disturbances. Among other fatty acids, palmitoleic and oleic acid have been shown to be important for sleep disorders, perhaps due to their function as precursors of the sleep inducing oleamide.

Example 26. A Case Study on Dental Diseases

[00102] In a vegetarian host subject, less dental sensitivity, reversal of gum receding, brightening of tooth enamel, and lessening of dental spots and plaque were observed when omega-3 fatty acids were reduced from 2 grams to 1.2 grams while holding omega-6 constant at 11 grams. Lipid compositions comprising nuts and oils were the source of omega-6 and omega-3 fatty acids. There was an adjustment period of 3-6 weeks, when the symptoms got worse in the host subjects before getting better. Longer-term intervention studies should be able to test the hypothesis by studying tooth loss during the intervention period. Bioactivity of lipids may explain the linkage between periodontitis/tooth loss and coronary heart disease.

Example 27. Case Studies on Immunity, Autoimmune and Infectious and Inflammatory Diseases

[00103] In a vegetarian host subject, a 48-year old menopausal woman, on 11g of linoleic acid (LA) and 1.8g of alpha-linolenic acid (ALA), from oils and nuts, spinal burning sensation, heat in the body, skin and feet, and delayed wound healing were observed. The subject also developed vaginal yeast infection.

Symptoms disappeared upon reducing ALA to 1.2g after an initial adjustment period. It is hypothesized that omega-6 and omega-3 fatty acid imbalance leads to inflammation, compromised immunity, and infection, particularly during the adjustment period following large changes in dietary fatty acids. It is further suspected that both omega-6 and omega-3 are anti-inflammatory in small doses and inflammatory in large doses, particularly in light of possible interactions with phytochemicals. In one embodiment, excessive suppression of the immune system through omega-3, phytochemicals, and other dietary constituents may lead to up-regulation of compensatory mechanisms causing dysregulated inflammation leading to a number of diseases. Therefore, it is an embodiment of this disclosure that net effect of all dietary immunomodulation below the threshold where self-regulation of the immune system is suppressed may be more effective nutritional approach.

[00104] It is understood that the total percent by weight of any combination of components does not exceed 100%. It is also understood that if a component is present in a composition, then the component is present in a non-zero amount (for example, more than about 0.00000001 mg or percent by weight of total weight).

[00105] The amounts and ratios of various nuts, seeds, lipids, and oil, to name a few, of the present embodiments were discovered to be beneficial, including by links to benefits for various diseases and conditions, as set forth above, empirically by outcome-focused experimentation. The above recited examples, case studies, links with particular medical conditions, and the like are not meant to limit the present disclosure, but merely to explain the disclosure by way of example.

[00106] While some embodiments of the present disclosure have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the disclosure. It should be understood that various alternatives to the embodiments of the disclosure described herein may be employed in practicing the disclosure. It is intended that the following claims define the scope of the disclosure and that methods and structures within the scope of these claims and their equivalents be covered thereby.

PENDING CLAIMS
(Without the withdrawn claims)

52. The formulation of claim 65, comprising one or more fatty acids selected from butyric acid (C4:0), lauric acid (C12:0), myristic acid (C14:0), palmitic acid (C16:0), stearic acid (C18:0), arachidic acid (C20:0), myristoleic acid (C14:1), palmitoleic acid (C16:1), oleic acid (C18:1), gadoleic acid (C20:1), ercucic acid (C22:1), nervonic acid (C24:1), linoleic acid (C18:2), conjugated-linoleic acid (C18:2), gamma-linolenic acid (C18:3), eicosadienoic acid (C20:2), di-homo-gamma-linolenic acid (C20:3), arachidonic acid (C20:4), alpha-linolenic acid (C18:3), stearidonic acid (C18:4), eicosapentaenoic acid (C20:5), docosapentaenoic acid (C22:5), and docosahexaenoic acid (C22:6).

61. The formulation of claim 65, wherein one or more of the following apply:

(i) comprising one or more of seeds, nuts, oils, legumes, dairy, cocoa, lentils, grains, culinary nuts and/or seeds in their whole form or their oils;
(ii) comprising oils, butters, nuts, seeds, herbs, sweeteners, and other foods, as source of fatty acids, antioxidants, minerals, and/or phytochemicals;
(iii) comprising one or more of peanut oil, corn oil, avocado oil, olive oil, sunflower oil, safflower oil, coconut oil, mustard oil, palm oil, soybean lecithin, and anhydrous butter;
(iv) comprising one or more of peanuts, almonds, olives, soybeans, cashews, flaxseeds, pistachios, pumpkin seeds, sunflower seeds, sesame seeds, walnuts, anhydrous butter**,** and coconut meat, or their oils; or
(v) comprising omega-6 fatty acids at 4% to 75% by weight and omega-3 fatty acids at 0.1% to 30% by weight of total lipids, and wherein the nuts or their oils comprise almonds, peanuts, and/or coconut meat, and the formulation optionally comprises anhydrous butter.

64. The formulation of claim 65, wherein the formulation is an enteral or parenteral formulation.

65. A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids from different sources, and wherein

(1) omega-6 fatty acids are 4-75% by weight of total lipids and omega-3 fatty acids are 0.1-30% by weight of total lipids; or
(2) omega-6 fatty acids are not more than 40 grams.

67. The formulation of claim 65, further comprising a source of carbohydrates, and a source of protein.

68. The formulation of claim 67, wherein one or more of the following apply:

(i) comprising 20-45% of a diet's calories from fat, 45-65% of a diet's calories from carbohydrates, and 10%-25% of a diet's calories from protein;

(ii) comprising carbohydrates calories of which 50-70% are from grains, 15-30% are from vegetables, and 10-30 % are from fruits, wherein optionally grains are selected from wheat, rice, corn, barley, spelt, oats, rye, buckwheat, millet, and quinoa; or

(iii) comprising protein calories of which less than 75% are from legumes, less than 25% are from eggs, less than 25% are from cheese, less than 25% are from milk, less than 25% are from yogurt, less than 30% are from poultry, less than 30% are from seafood, less than 30% are from meat, and less than 15% are from other sources.

69. The formulation of claim 65, wherein one or more of the following apply:

(i) comprising one or more polyphenols selected from: a flavonoid, a flavonol, a flavanone, an isoflavone, an anthocyanidin, a phytoestrogen, a catechin, a quercetin, resveratrol, a lignan, gallic acid, ellagic acid, and curcumin;

(ii) comprising one or more phytochemicals selected from: phytosterols, campesterol, sitosterol, and stigmasterol, organosulfur, sulfide, melatonin, carotenoid, beta carotene, lycopene, lutein, zeaxanthin, and a phenol;

(iii) comprising dosage of phytosterols less than 150mg;

(iv) comprising one or more of: dosage of campesterol less than 1.5mg, dosage of sitosterol less than 30mg, and dosage of stigmasterol less than 1.5mg;

(v) comprising one or more phytochemicals, antioxidants, vitamins, minerals, and trace elements;

(vi) comprising one or more of: dosage of vitamin A less than 30000IU, dosage of folic acid or folate less than 800mcg, dosage of vitamin C less than 400mg, dosage of vitamin D less than 400IU, dosage of vitamin E tocopherol beta less than 0.5mg, dosage of vitamin E tocopherol delta less than 0.5mg, dosage of vitamin E tocopherol gamma less than 4mg, dosage of vitamin E tocopherol alpha less than 15mg, dosage of copper less than 3mg, dosage of zinc less than 14mg, dosage of manganese less than 8mg, dosage of iron less than18mg, dosage of selenium less than 80mcg, and dosage of magnesium less than 700mg;

(vii) comprising one or more of: dosage of alpha carotene less than 4000mcg, dosage of beta carotene less than 14000mcg, dosage of beta cryptoxanthin less than 850mcg, dosage of betaine less than 50mg, dosage of choline less than 250mg, dosage of lycopene less than 1900 mcg, and dosage of lutein/zeaxanthin less than 14000mcg;

(viii) comprising vitamin E in the range of 0.001 % to 0.5% by weight of total lipids; or
(ix) comprising a dosage of fiber less than 45g.

73. The formulation of claim 65, whereby the lipid-containing formulation provides a substitution and/or supplementation of lipids that are typically added to food preparations so that when the formulation is provided in combination with a lipid-free or low-lipid food product, the combination of the formulation and the food preparation provides a balanced lipid intake to the subject ingesting the combination.

74. The formulation of claim 65, whereby the formulation supplies 60-90% of a diet's fat calories.

75. The formulation of claim 65, wherein the formulation is in the form of a liquid, semi-solid, solid, granule, powder, capsule, tablet, lozenge, pill, or combination thereof.

77. The formulation of claim 65, wherein the formulation is one-part or comprises multi-part mutually complementing components, for one or more days, one or more weeks, or one or more months.

78. The formulation of claim 65, whereby the formulation provides gradual and/or steady delivery so that any omega-3 withdrawal is gradual, and/or any omega-6 and/or other fatty acid increase is gradual.

80. The formulation of claim 65, further comprising a source of nutrients selected from one or more of grains, legumes, fruits, vegetables, yogurt, herbs, spices, sweeteners, eggs, cheese, milk, poultry, seafood, and meat.

82. The formulation of claim 65, wherein
(i) the omega-6 to omega-3 ratio is greater than 6:1; or
(ii) the omega-6 to omega-3 ratio is at least 9:1.

83. The formulation of claim 65, wherein one or more of the following apply:
(i) the formulation of (2) wherein omega-6 fatty acids are present at 4% to 75% by weight of total lipids;
(ii) the formulation of (2) wherein omega-3 fatty acids are present at 0.1% to 30% by weight of total lipids;
(iii) the dosage of eicosapentaenoic acid (C20:5) is not more than 0.5 grams, and/or the dosage of docosahexaenoic acid (C22:6) is not more than 0.2 grams; or
(iv) omega-9 fatty acids are present at 10% to 90% by weight of total lipids.

90. The formulation of claim 65, whereby one or more nutrients are effective to provide a therapeutic effect comprising prophylaxis or alleviation of one or more symptoms associated with a disease or condition selected from the group consisting of: menopause, aging, musculoskeletal disorders, hypercholesterolemia, mood swing, reduced cognitive function, neural disorders, mental disorders, thyroid disturbances, weight gain, obesity, diabetes, endocrine disorders, digestive system disorders, reproductive disorders, pulmonary disorders, renal diseases, ophthalmologic disorders, dermatological disorders, sleep disorders, dental diseases, cancer, autoimmune diseases, infectious diseases, inflammatory diseases, dyslipidemia and cardiovascular disease.

91. A lipid-containing formulation, comprising a dosage of omega-6 fatty acids, wherein the omega-6 fatty acids are greater than 20% by weight of the total lipids, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids from different sources, the formulation comprising polyunsaturated, monounsaturated, and saturated fatty acids, and wherein the formulation includes at least

(i) one or more polyunsaturated fatty acids selected from linoleic acid (C18:2), conjugated-linoleic acid (C18:2), gamma-linolenic acid (C18:3), eicosadienoic acid (C20:2), di-homo-gamma-linolenic acid (C20:3), arachidonic acid (C20:4), alpha-linolenic acid (C18:3), stearidonic acid (C18:4), eicosapentaenoic acid (C20:5), docosapentaenoic acid (C22:5), and docosahexaenoic acid (C22:6), and

(ii) nutrients including at least

(a) one or more polyphenols, or

(b) one or more phytochemicals,

the one or more phytochemicals being selected from: phytosterols, campesterol, sitosterol, stigmasterol, organosulfur, sulfide, melatonin, lycopene, lutein, zeaxanthin, and a phenol.

92. The formulation of claim 65, wherein the formulation provides 40 grams or less of omega-6 dosage.

93. The formulation of claim 65, wherein the dosage of omega-6 fatty acids is from 1 to 10 grams, or from 2 to15 grams, or from 2 to 25 grams, or from 2 to 40 grams.

94. The formulation of claim 65, wherein the dosage of total fat in grams is from 10-100 grams, 10-75 grams, or 20-100 grams.

95. The formulation of claim 65, wherein the dosage of omega-3 fatty acids is from 0.1 to 1.0 grams, or from 0.2 to 1.0 grams, or from 1.0 to 2.0 grams, or from 2.0 to 3.0 grams, or from 2.0 to 4.0 grams or from 2.0 to 6.0 grams.

96. The formulation of claim 65, wherein the formulation comprises one or more nutrients effective to provide beneficial effects at omega-6 to omega-3 ratio of at least 4:1, and/or one or more nutrients at amounts effective to reduce omega-3 requirements and/or allow for higher omega-6 to omega-3 ratio than in the absence of the nutrient and/or increase effective levels of omega-3 in the subject.

97. The formulation of claim 65, wherein the formulation comprises one or more polyphenols, and is effective to increase omega-3 levels in the subject.

98. The formulation of claim 65, wherein the formulation comprises daily amounts of fatty acids for the subject based on one or more factors selected from: age of the subject, sex of the subject, diet of the subject, the body weight of the subject, physical activity level of the subject, lipid tolerance of the subject, medical conditions of the subject, family medical history of the subject, and climate of the subject's living area.

99. The formulation of claim 91, wherein omega-3 fatty acids are present at 0.1% to 30% by weight of total lipids; the dosage of eicosapentaenoic acid (C20:5) is not more than 0.5 grams, and/or the dosage of docosahexaenoic acid (C22:6) is not more than 0.2 grams; and/or omega-9 fatty acids are present at 10% to 90% by weight of total lipids.

100. The formulation of claim 65, wherein the ratio of total fatty acids to monounsaturated fatty acids is in the range of 1:1 to 15:1; the ratio of total fatty acids to saturated fatty acids is in the range of 1:1 to 15:1; and/or the ratio of monounsaturated fatty acids to polyunsaturated fatty acids is in the range of 0.25:1 to 6:1.

101. The formulation of claim 91, wherein the ratio of total fatty acids to monounsaturated fatty acids is in the range of 1:1 to 15:1; the ratio of total fatty acids to saturated fatty acids is in the range of 1:1 to 15:1; and/or the ratio of monounsaturated fatty acids to polyunsaturated fatty acids is in the range of 0.25:1 to 6:1.

102. The formulation of claim 65, wherein the dosage of total fat is 10-100 grams, the dosage of omega-6 fatty acids is from 1 to 40 grams; the dosage of omega-3 fatty acids is from 0.1 to 5 grams, the ratio of monounsaturated fatty acids to polyunsaturated fatty acids is in the range of 1:1 to 3:1, the ratio of monounsaturated fatty acids to saturated fatty acids is 1:1 to 5:1, the ratio of omega-9 to omega-6 fatty acids is in the range of 1:1-3:1, and the ratio of omega-6 to omega-3 fatty acids is in the range of 4:1 to 45:1.

107. The formulation of claim 98, wherein the fatty acid content is as set forth in Tables 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20.

116. The formulation of claim 91, comprising one or more fatty acids selected from butyric acid (C4:0), lauric acid (C12:0), myristic acid (C14:0), palmitic acid (C16:0), stearic acid (C18:0), arachidic acid (C20:0), myristoleic acid (C14:1), palmitoleic acid (C16:1), oleic acid (C18:1), gadoleic acid (C20:1), ercucic acid (C22:1), nervonic acid (C24:1), linoleic acid (C18:2), conjugated-linoleic acid (C18:2), gamma-linolenic acid (C18:3), eicosadienoic acid (C20:2), di-homo-gamma-linolenic acid (C20:3), arachidonic acid (C20:4), alpha-linolenic acid (C18:3), stearidonic acid (C18:4), eicosapentaenoic acid (C20:5), docosapentaenoic acid (C22:5), and docosahexaenoic acid (C22:6).

117. The formulation of claim 91, wherein one of the following apply:
(i) comprising omega-6 and omega-3 fatty acids wherein the omega-6 to omega-3 ratio is 4:1 to 45:1; or
(ii) comprising omega-6 and omega-3 fatty acids wherein the omega-6 to omega-3 ratio is at least 9:1.

118. The formulation of claim 91, wherein one or more of the following apply:
(i) the dosage of total lipids is from 10-100 grams;
(ii) the formulation comprises less than 40 grams of dosage of omega-6 fatty-acids;
(iii) the dosage of omega-6 fatty acids is from 1 to 40 grams;
(iv) the dosage of omega-3 fatty acids is from 0.1 to 6.0 grams;
(v) the dosage of total of lipids is 10-100 grams, dosage of omega-6 fatty acids is from 1 to 40 grams, dosage of omega-3 fatty acids is from 0.1 to 5 grams, the ratio of monounsaturated fatty acids to polyunsaturated fatty acids is in the range of 1:1 to 3:1, the ratio of monounsaturated fatty acids to saturated fatty acids is 1:1 to 5:1, the ratio of omega-9 to omega-6 fatty acids is in the range of 1:1 to 3:1, and the ratio of omega-6 to omega-3 fatty acids is in the range of 4:1 to 45:1;
(vi) whereby the formulation supplies 60-90% of a diet's fat calories; or
(vii) the formulation is adapted for use in combination with or provided with a lipid-free or low-lipid food product.

119. The formulation of claim 91, wherein the fatty acid content is as set forth in Tables 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20.

120. The formulation of claim 91, wherein one or more of the following apply:
(i) comprising one or more polyphenols selected from: a flavonoid, a flavonol, a flavanone, an isoflavone, an anthocyanidin, a phytoestrogen, a catechin, a quercetin, resveratrol, a lignan, gallic acid, ellagic acid, and curcumin;
(ii) comprising dosage of phytosterols less than 150mg;
(iii) comprising one or more of: dosage of campesterol less than 1.5mg, dosage of sitosterol less than 30mg, and dosage of stigmasterol less than 1.5mg;

(iv) comprising one or more phytochemicals, antioxidants, vitamins, minerals, and trace elements;
(v) comprising one or more of: dosage of vitamin A less than 30000IU, dosage of folic acid or folate less than 800mcg, dosage of vitamin C less than 400mg, dosage of vitamin D less than 400IU, dosage of vitamin E tocopherol beta less than 0.5mg, dosage of vitamin E tocopherol delta less than 0.5mg, dosage of vitamin E tocopherol gamma less than 4mg, dosage of vitamin E tocopherol alpha less than 15mg, dosage of copper less than 3mg, dosage of zinc less than 14mg, dosage of manganese less than 8mg, dosage of iron less than18mg, dosage of selenium less than 80mcg, and dosage of magnesium less than 700mg;
(vi) comprising one or more of: dosage of alpha carotene less than 4000mcg, dosage of beta carotene less than 14000mcg, dosage of beta cryptoxanthin less than 850mcg, dosage of betaine less than 50mg, dosage of choline less than 250mg, dosage of lycopene less than 1900 mcg, and dosage of lutein/zeaxanthin less than 14000mcg;
(vii) comprising vitamin E in the range of 0.001 % to 0.5% by weight of total lipids; or
(viii) comprising a dosage of fiber less than 45g.

121. The formulation of claim 91, wherein one or more of the following apply:
(i) comprising a source of nutrients selected from one or more of grains, legumes, fruits, vegetables, yogurt, herbs, spices, sweeteners, eggs, cheese, milk, poultry, seafood, and meat;
(ii) comprising 20-45% of a diet's calories from fat, 45-65% of a diet's calories from carbohydrates, and 10%-25% of a diet's calories from protein;
(iii) comprising carbohydrates calories of which 50-70% are from grains, 15-30% are from vegetables, and 10-30 % are from fruits, wherein optionally grains are selected from wheat, rice, corn, barley, spelt, oats, rye, buckwheat, millet, and quinoa; or
(iv) comprising protein calories of which less than 75% are from legumes, less than 25% are from eggs, less than 25% are from cheese, less than 25% are from milk, less than 25% are from yogurt, less than 30% are from poultry, less than 30% are from seafood, less than 30% are from meat, and less than 15% are from other sources.

122. The formulation of claim 91, wherein the formulation comprises daily amounts of fatty acids for the subject based on one or more factors selected from: age of the subject, sex of the subject, diet of the subject, the body weight of the subject, physical activity level of the subject, lipid tolerance of the subject, medical conditions of the subject, family medical history of the subject, and climate of the subject's living area.

124. The formulation of claim 91, wherein the formulation is configured for administration by gradual and/or steady delivery.

128. The formulation of claim 91, wherein the formulation is selected from:

(1) a formulation wherein omega-6 fatty acids are present at 4% to 75% by weight, and omega-3 fatty acids are present at 0.1% to 30% by weight, and wherein the formulation comprises nuts or their oils, wherein said nuts or their oils are obtained from almonds, peanuts, and/or coconut meat, and the formulation optionally comprises anhydrous butter;

(2) a formulation comprising:

a peanut oil present at 8 to 56 percent by weight in the formulation; and at least two of: a vegetable oil present at 8 to 46 percent by weight in the formulation, wherein the vegetable oil is selected from one or more of acai oil, amaranth oil, apple seed oil, apricot kernel oil, argan oil, artichoke oil, babassu oil, ben oil, blackcurrant seed oil, borage seed oil, borneo tallow nut oil, bottle gourd oil, buffalo gourd oil, canola oil (rapeseed), cape chestnut oil, carob pod oil, cocklebur oil, cocoa butter oil, cohune oil, coriander seed oil, corn oil, cottonseed oil, dika oil, evening primrose oil, false flax oil (*Camelina sativa*), grapeseed oil, kapok seed oil, lallemantia oil, marula oil, meadowfoam seed oil, mustard oil, nutmeg butter, okra seed oil, palm oil, papaya seed oil, pequi oil, perilla oil, prune kernel oil, quinoa oil, ramtil oil, rice bran oil, royle oil, sacha inchi oil, sheanut oil, soybean lecithin oil, tea oil, thistle oil, tomato seed oil, ucuhuba butter oil, wheat germ oil, acorn oil, almond oil, beech nut oil, brazilnut oil, breadnut oil, candlenut oil, chestnut oil, chilacayote nut oil, chilean hazelnut oil, coconut oil, cashew oil, colocynth nut oil, filbert oil, hazelnut oil, hickory oil, kola nut oil, macadamia oil, mamoncillo oil, mongongo oil, obongo nut oil, pecan oil, pili nut oil, pine nut oil, pistachio oil, soya oil, poppy seed oil, pumpkin seed oil, hemp seed oil, flax seed oil, sesame seed oil, walnut oil, and watermelon seed oil;

an avocado oil present at 3 to 16 percent by weight in the formulation;

an olive oil present at 5 to 32 percent by weight in the formulation;

a sunflower oil present at 6 to 34 percent by weight in the formulation; and

a safflower oil present at 2 to 30 percent by weight in the formulation;

(3) a formulation comprising three or more of:

an almond oil present at 2 to 23 percent by weight in the formulation;

an avocado oil present at 1 to 7 percent by weight in the formulation;

a soybean oil present at 1 to 7 percent by weight in the formulation;

a cashew oil present at 2 to 15 percent by weight in the formulation;

a pistachio oil present at 1 to 7 percent by weight in the formulation;

a pumpkin seed oil present at 1 to 8 percent by weight in the formulation;

a walnut oil present at 3 to 25 percent by weight in the formulation;

a peanut oil present at 5 to 30 percent by weight in the formulation;

a corn oil present at 3 to 19 percent by weight in the formulation;

an olive oil present at 3 to 17 percent by weight in the formulation;

a safflower oil present at 1 to 14 percent by weight in the formulation; and

an anhydrous butter present at 5 to 29 percent by weight in the formulation; or

(4) a formulation comprising three or more of:
an almond oil present at 1 to 36 percent by weight in the formulation;
a pumpkin seed oil present at 1 to 24 percent by weight in the formulation;
an oil from walnuts present at 2 to 36 percent by weight in the formulation;
a peanut oil present at 4 to 72 percent by weight in the formulation;
a corn oil present at 1 to 24 percent by weight in the formulation;
an olive oil present at 2 to 36 percent by weight in the formulation;
a sunflower oil present at 4 to 72 percent by weight in the formulation;
a safflower oil present at 2 to 60 percent by weight in the formulation; and
an anhydrous butter present at 2 to 36 percent by weight in the formulation;
further comprising one or more of:
a mustard oil present at 8 percent or less by weight in said formulation,
a palm oil present at 2 percent or less by weight in said formulation,
a flaxseed oil at 8 percent or less by weight in said formulation,
a coconut oil present at 8 percent or less by weight in said formulation, and
a soybean lecithin present at 4 percent or less by weight in said formulation;

(5) a formulation comprising three or more of:
peanuts present at 2 to 11 percent by weight in the formulation;
almonds present at 5 to 32 percent by weight in the formulation;
olives present at 6 to 36 percent by weight in the formulation;
soybeans present at 4 to 25 percent by weight in the formulation;
cashews present at 4 to 21 percent by weight in the formulation;
pistachios present at 2 to 9 percent by weight in the formulation;
pumpkin seeds present at 2 to 15 percent by weight in the formulation;
sunflower seeds present at 1 to 4 percent by weight in the formulation;
walnuts present at 3 to 25 percent by weight in the formulation;
anhydrous butter present at 4 to 24 percent by weight in the formulation; and
coconut meat present at 1 to 6 percent by weight in the formulation;

(6) a formulation comprising at least three of safflower oil, sunflower oil, peanut oil, almond or almond oil, corn oil, and anhydrous butter; and

(7) a formulation comprising three or more of peanuts, almonds, olives, soybeans, cashews, flaxseeds, pistachios, pumpkin seeds, sunflower seeds, sesame seeds, walnuts, and coconut meat, or their oils.

129. A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of fatty acids from different sources; and wherein

omega-6 fatty acids are 4-75% by weight of total lipids and omega-3 fatty acids are 0.1-30% by weight of total lipids.

130. A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of fatty acids from different sources; and wherein

omega-6 fatty acids are not more than 40 grams and the formulation further comprises one or more polyphenols, or one or more phytochemicals selected from: phytosterols, campesterol, sitosterol, stigmasterol, organosulfur, a sulfide, melatonin, lycopene, lutein, and zeaxanthin, or vitamin E-alpha/gamma less than 0.5% by weight of total lipids, or one or more specific protein types listed in Table 21 in a dosage not more than the upper limit disclosed in the table.

131. The formulation of claim 65, wherein the omega-6 to omega-3 ratio is 4:1 to 45:1.

132. The formulation of claim 91, wherein the nutrients include at least the one or more polyphenols and the one or more phytochemicals.

133. The formulation of claim 65, wherein the formulation is in the form of full meal or dietary component selected from an oil, a gel, sauce, spread, butter, dressing, side dish, snack, salad, nutritional bar, bread, dessert, chocolate, fudge, pastry, truffle, pudding, cake, bakery product, yogurt, drink, and combinations thereof.

134. The formulation of claim 91, wherein one or more of the following apply:

(i) the formulation is in the form of full meal or a dietary component selected from an oil, gel, sauce, dressing, spread, butter, drops, nutritional bar, snack, bread, bakery product, dairy product, side dish, salad, dessert, chocolate, fudge, pastry, truffle, pudding, cake, yogurt, drink, and combinations thereof; or

(ii) the formulation is in the form of enteral, parenteral, a liquid, a semi-solid, a solid, capsule, tablet, granule, powder, lozenge, pill, or a combination thereof; or

(iii) the formulation is one-part or comprises multi-part mutually complementing components, for one or more days, one or more weeks, or one or more months.

135. The formulation of claim 65, wherein one or more dosages are therapeutically effective.

136. The formulation of claim 65, wherein the formulation includes one or more carriers selected from starches, sugars, granulating agents, binders and disintegrating agents.

137. The formulation of claim 65, wherein the formulation is for a human infant, or adult.

138. The formulation of claim 91, wherein one or more dosages are therapeutically effective.

139. The formulation of claim 91, wherein the formulation includes one or more carriers selected from starches, sugars, diluents, granulating agents, binders and disintegrating agents.

140. The formulation of claim 91, wherein the formulation is for a human infant, adult, or child.

141. The formulation of claim 91, wherein one or more of the following apply:

(i) comprising one or more nutrients effective to reduce omega-3 requirement and/or allow for higher omega-6 to omega-3 ratio than in the absence of the nutrient and/or increase effective levels of omega-3 in the subject; or

(ii) comprising one or more polyphenols effective to increase omega-3 levels in the subject.

142. The formulation of claim 65, wherein one or more of the following apply:

(i) the lipids in the intermixture are fatty acids in their free form;
(ii) the lipids in the intermixture are fatty acids in their ester form;
(iii) the lipids in the intermixture are in their isolated form;
(iv) the sources of lipids include butters, nuts, seeds, herbs, and/or sweeteners;
(v) the lipids from different sources are wherein lipid profile of two or more sources intermixed are different from each other;
(vi) the lipids from different sources are wherein different lipids from different sources are intermixed synergistically; or
(vii) excess delivery of lipids from a single source is avoided.

143. The formulation of claim 91, wherein one or more of the following apply:

(i) the lipids in the intermixture are fatty acids in their free form;
(ii) the lipids in the intermixture are fatty acids in their ester form;
(iii) the lipids in the intermixture are in their isolated form;
(iv) the sources of lipids include butters, nuts, seeds, herbs, and/or sweeteners;

(v) the lipids from different sources are wherein lipid profile of two or more sources intermixed are different from each other;
(vi)) the lipids from different sources are wherein different lipids from different sources are intermixed synergistically; or
(vii) excess delivery of lipids from a single source is avoided.

144. The formulation of claim 65, wherein one or more of the following apply:

(i) the intermixture is a gel;
(ii) the intermixture is a powder;
(iii) the intermixture is solid;
(iv) the intermixture is semi-solid; or
(v) the intermixture is a blend.

145. The formulation of claim 91, wherein one or more of the following apply:

(i) the intermixture is a gel;
(ii) the intermixture is a powder;
(iii) the intermixture is solid;
(iv) the intermixture is semi-solid; or
(v) the intermixture is a blend.

NOTE: Claims 1-51, 53-60, 62-63, 66, 70-72, 76, 79, 81, 84-89, 106, 110, 112, and 123 are cancelled, and claims 103-105, 108-109, 111, 113-115, and 125-127 are withdrawn.

LIPID CONTAINING COMPOSITIONS AND METHODS OF USE THEREOF

ABSTRACT OF THE DISCLOSURE

Lipid compositions comprising nuts, seeds, oils, legumes, fruits, grains, and dairy useful in specified amounts as dietary supplements and diet plans designed around and including the aforementioned for the prophylaxis and treatment of numerous diseases are disclosed. The compositions include omega-6 and omega-3 fatty acids where the ratio of the omega-6 to the omega-3 fatty acids and their amounts are controlled based on one or more factors including age of the subject, sex of the subject, diet of the subject, the body weight of the subject, medical conditions of the subject, and climate of the subject's living area.

ANNEX B:

Cited art "Olive oil" webpages from
http://nutritiondata.self.com/facts/fats-and-oils/509/2 (accessed
February 11, 2015)

SELFNutritionData

Oil, olive, salad or cooking

FOOD SUMMARY

Nutrition Facts

Serving Size 1 ounce (28g)

Amount Per Serving

Calories 248 Calories from Fat 248

% Daily Value*

Total Fat 28g 43%

Saturated Fat 4g 19%

Trans Fat

Cholesterol 0mg 0%

Sodium 1mg 0%

Total Carbohydrate 0g 0%

Dietary Fiber 0g 0%

Sugars 0g

Protein 0g

Vitamin A 6% • Vitamin C 0%

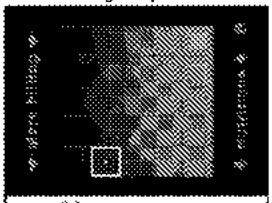
Calcium 0% • Iron 1%

*Percent Daily Values are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs.

NutritionData.com

Download Printable Label Image

Nutritional Target Map

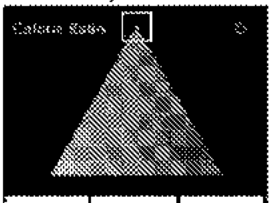


0.8

1.4

Fullness Factor | ND Rating

Caloric Ratio Pyramid



0% | 100% | 0%

Carbs | Fats | Protein

NutritionData's Opinion

0

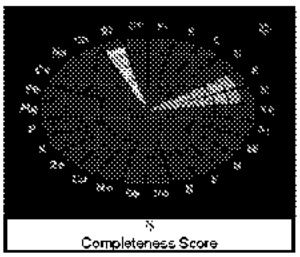
Weight loss:

Optimum health:

Weight gain:

The good: This food is very low in Cholesterol and Sodium

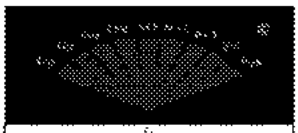
NUTRIENT BALANCE



%

Completeness Score

PROTEIN QUALITY



%

Amino Acid Score

NUTRITION INFORMATION

Amounts per 1 ounce (28g)

Calorie Information

Amounts Per Selected Serving		%DV
Calories	248 (1038 kJ)	12%
From Carbohydrate	0.0 (0.0 kJ)	
From Fat	248 (1038 kJ)	
From Protein	0.0 (0.0 kJ)	
From Alcohol	0.0 (0.0 kJ)	

Carbohydrates

Amounts Per Selected Serving		%DV
Total Carbohydrate	0.0 g	0%
Dietary Fiber	0.0 g	0%
Starch	0.0 g	
Sugars	0.0 g	
Sucrose	0.0 mg	
Glucose	0.0 mg	
Fructose	0.0 mg	
Lactose	0.0 mg	

Protein & Amino Acids

Amounts Per Selected Serving		%DV
Protein	0.0 g	0%
Tryptophan	0.0 mg	
Threonine	0.0 mg	
Isoleucine	0.0 mg	
Leucine	0.0 mg	
Lysine	0.0 mg	
Methionine	0.0 mg	
Cystine	0.0 mg	
Phenylalanine	0.0 mg	
Tyrosine	0.0 mg	
Valine	0.0 mg	
Arginine	0.0 mg	
Histidine	0.0 mg	
Alanine	0.0 mg	
Aspartic acid	0.0 mg	
Glutamic acid	0.0 mg	
Glycine	0.0 mg	
Proline	0.0 mg	
Serine	0.0 mg	
Hydroxyproline	0.0 mg	

Maltose	0.0 mg
Galactose	0.0 mg

Fats & Fatty Acids

Amounts Per Selected Serving		%DV
Total Fat	28.0 g	43%
Saturated Fat	3.9 g	19%
4:00	0.0 mg	
6:00	0.0 mg	
8:00	0.0 mg	
10:00	0.0 mg	
12:00	0.0 mg	
13:00	~	
14:00	0.0 mg	
15:00	~	
16:00	3161 mg	
17:00	6.2 mg	
18:00	547 mg	
19:00	~	
20:00	116 mg	
22:00	36.1 mg	
24:00:00	0.0 mg	
Monounsaturated Fat	20.4 g	
14:01	0.0 mg	
15:01	~	
16:1 undifferentiated	351 mg	
16:1 c	~	
16:1 t	~	
17:01	35.0 mg	
18:1 undifferentiated	19954 mg	
18:1 c	~	
18:1 t	~	
20:01	87.1 mg	
22:1 undifferentiated	0.0 mg	
22:1 c	~	
22:1 t	~	
24:1 c	~	
Polyunsaturated Fat	2.9 g	
16:2 undifferentiated	~	
18:2 undifferentiated	2734 mg	
18:2 n-6 c,c	~	
18:2 c,t	~	
18:2 t,c	~	
18:2 t,t	~	
18:2 i	~	
18:2 t not further defined	~	
18:03	213 mg	
18:3 n-3, c,c,c	~	
18:3 n-6, c,c,c	~	
18:4 undifferentiated	0.0 mg	
20:2 n-6 c,c	~	
20:3 undifferentiated	~	
20:3 n-3	~	
20:3 n-6	~	
20:4 undifferentiated	0.0 mg	
20:4 n-3	~	
20:4 n-6	~	
20:5 n-3	0.0 mg	
22:02	~	
22:5 n-3	0.0 mg	
22:6 n-3	0.0 mg	
Total trans fatty acids	~	
Total trans-monoenoic fatty acids	~	
Total trans-polyenoic fatty acids	~	
Total Omega-3 fatty acids	213 mg	
Total Omega-6 fatty acids	2734 mg	

Learn more about these fatty acids and their equivalent names

Vitamins

Amounts Per Selected Serving		%DV
Vitamin A	0.0 IU	0%
Retinol	0.0 mcg	
Retinol Activity Equivalent	0.0 mcg	
Alpha Carotene	0.0 mcg	
Beta Carotene	0.0 mcg	
Beta Cryptoxanthin	0.0 mcg	
Lycopene	0.0 mcg	
Lutein+Zeaxanthin	0.0 mcg	
Vitamin C	0.0 mg	0%
Vitamin D	~	~
Vitamin E (Alpha Tocopherol)	4.0 mg	20%
Beta Tocopherol	0.0 mg	
Gamma Tocopherol	0.2 mg	
Delta Tocopherol	0.0 mg	
Vitamin K	16.9 mcg	21%
Thiamin	0.0 mg	0%
Riboflavin	0.0 mg	0%
Niacin	0.0 mg	0%
Vitamin B6	0.0 mg	0%
Folate	0.0 mcg	0%
Food Folate	0.0 mcg	
Folic Acid	0.0 mcg	
Dietary Folate Equivalents	0.0 mcg	
Vitamin B12	0.0 mcg	0%
Pantothenic Acid	0.0 mg	0%
Choline	0.1 mg	
Betaine	0.0 mg	

Minerals

Amounts Per Selected Serving		%DV
Calcium	0.3 mg	0%
Iron	0.2 mg	1%
Magnesium	0.0 mg	0%
Phosphorus	0.0 mg	0%
Potassium	0.3 mg	0%
Sodium	0.6 mg	0%
Zinc	0.0 mg	0%
Copper	0.0 mg	0%
Manganese	0.0 mg	0%
Selenium	0.0 mcg	0%
Fluoride	~	

Sterols

Amounts Per Selected Serving		%DV
Cholesterol	0.0 mg	0%
Phytosterols	61.9 mg	
Campesterol	~	
Stigmasterol	~	
Beta-sitosterol	~	

Other

Amounts Per Selected Serving		%DV
Alcohol	0.0 g	
Water	0.0 g	
Ash	0.0 g	
Caffeine	0.0 mg	
Theobromine	0.0 mg	

Footnotes for Oil, olive, salad or cooking

Source. Nutrient data for this listing was provided by USDA SR-21. Each "~" indicates a missing or incomplete value.

Percent Daily Values (%DV) are for adults or children aged 4 or older, and are based on a 2,000 calorie reference diet. Your daily values may be higher or lower based on your individual needs.

Nutrition Data's Opinion, Completeness Score™, Fullness Factor™, Rating, Estimated Glycemic Load (eGL), and Better Choices Substitutions™ are editorial opinions of NutritionData.com, given without warranty, and are not intended to replace the advice of a nutritionist or health-care professional. Nutrition Data's opinions and ratings are based on weighted averages of the nutrient densities of those nutrients for which the FDA has established Daily Values, and do not consider other nutrients that may be important to your health or take into account your individual needs. Consequently, Nutrition Data's higher-rated foods may not necessarily be healthier for you than lower-rated ones. All foods, regardless of their rating, have the potential to play an important role in your diet.

The Amino Acid Score has not been corrected for digestibility, which could reduce its value

ANNEX C:

Cited art "Walnut oil" webpages from http://nutritiondata.self.com/facts/fats-and-oils/589/2 (accessed February 11, 2015)

SELFNutritionData

Oil, vegetable, walnut

FOOD SUMMARY

Nutrition Facts

Serving Size 1 ounce (28g)

Amount Per Serving

Calories 248 Calories from Fat 248

% Daily Value*

Total Fat 28g 43%

Saturated Fat 3g 13%

Trans Fat

Cholesterol 0mg 0%

Sodium 0mg 0%

Total Carbohydrate 0g 0%

Dietary Fiber 0g 0%

Sugars 0g

Protein 0g

Vitamin A 6% • Vitamin C 0%

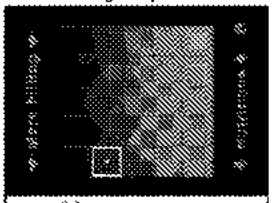
Calcium 0% • Iron 2%

*Percent Daily Values are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs.

NutritionData.com

Download Printable Label Image

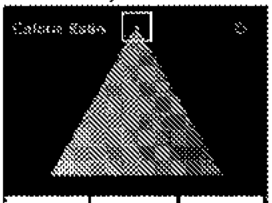
Nutritional Target Map



0.0 | 1.0

Fullness Factor | ND Rating

Caloric Ratio Pyramid



0% | 100% | 0%

Carbs | Fats | Protein

NutritionData's Opinion

Weight loss:

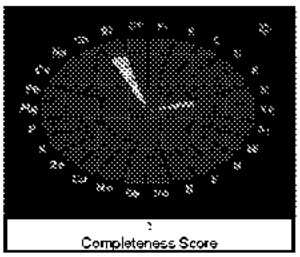
Optimum health:

Weight gain:

The good: This food is very low in Cholesterol and Sodium

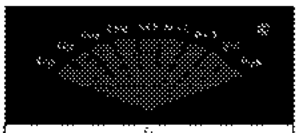
0

NUTRIENT BALANCE



Completeness Score

PROTEIN QUALITY



Amino Acid Score

NUTRITION INFORMATION

Amounts per 1 ounce (28g)

Calorie Information

Amounts Per Selected Serving		%DV
Calories	248 (1038 kJ)	12%
From Carbohydrate	0.0 (0.0 kJ)	
From Fat	248 (1038 kJ)	
From Protein	0.0 (0.0 kJ)	
From Alcohol	0.0 (0.0 kJ)	

Carbohydrates

Amounts Per Selected Serving		%DV
Total Carbohydrate	0.0 g	0%
Dietary Fiber	0.0 g	0%
Starch	0.0 g	
Sugars	0.0 g	
Sucrose	0.0 mg	
Glucose	0.0 mg	
Fructose	0.0 mg	
Lactose	0.0 mg	

Protein & Amino Acids

Amounts Per Selected Serving		%DV
Protein	0.0 g	0%
Tryptophan	0.0 mg	
Threonine	0.0 mg	
Isoleucine	0.0 mg	
Leucine	0.0 mg	
Lysine	0.0 mg	
Methionine	0.0 mg	
Cystine	0.0 mg	
Phenylalanine	0.0 mg	
Tyrosine	0.0 mg	
Valine	0.0 mg	
Arginine	0.0 mg	
Histidine	0.0 mg	
Alanine	0.0 mg	
Aspartic acid	0.0 mg	
Glutamic acid	0.0 mg	
Glycine	0.0 mg	
Proline	0.0 mg	
Serine	0.0 mg	
Hydroxyproline	0.0 mg	

Maltose	0.0 mg
Galactose	0.0 mg

Fats & Fatty Acids

Amounts Per Selected Serving		%DV
Total Fat	28.0 g	43%
Saturated Fat	2.5 g	13%
4:00	0.0 mg	
6:00	0.0 mg	
8:00	0.0 mg	
10:00	0.0 mg	
12:00	0.0 mg	
13:00	~	
14:00	0.0 mg	
15:00	~	
16:00	1960 mg	
17:00	~	
18:00	560 mg	
19:00	~	
20:00	~	
22:00	~	
24:00:00	~	
Monounsaturated Fat	6.4 g	
14:01	~	
15:01	~	
16:1 undifferentiated	28.0 mg	
16:1 c	~	
16:1 t	~	
17:01	~	
18:1 undifferentiated	6215 mg	
18:1 c	~	
18:1 t	~	
20:01	112 mg	
22:1 undifferentiated	0.0 mg	
22:1 c	~	
22:1 t	~	
24:1 c	~	
Polyunsaturated Fat	17.7 g	
16:2 undifferentiated	~	
18:2 undifferentiated	14810 mg	
18:2 n-6 c,c	~	
18:2 c,t	~	
18:2 t,c	~	
18:2 t,t	~	
18:2 i	~	
18:2 t not further defined	~	
18:03	2912 mg	
18:3 n-3, c,c,c	~	
18:3 n-6, c,c,c	~	
18:4 undifferentiated	0.0 mg	
20:2 n-6 c,c	~	
20:3 undifferentiated	~	
20:3 n-3	~	
20:3 n-6	~	
20:4 undifferentiated	0.0 mg	
20:4 n-3	~	
20:4 n-6	~	
20:5 n-3	0.0 mg	
22:02	~	
22:5 n-3	0.0 mg	
22:6 n-3	0.0 mg	
Total trans fatty acids	~	
Total trans-monoenoic fatty acids	~	
Total trans-polyenoic fatty acids	~	
Total Omega-3 fatty acids	2912 mg	
Total Omega-6 fatty acids	14810 mg	

Learn more about these fatty acids and their recommended ranges

Vitamins

Amounts Per Selected Serving		%DV
Vitamin A	0.0 IU	0%
Retinol	0.0 mcg	
Retinol Activity Equivalent	0.0 mcg	
Alpha Carotene	0.0 mcg	
Beta Carotene	0.0 mcg	
Beta Cryptoxanthin	0.0 mcg	
Lycopene	0.0 mcg	
Lutein+Zeaxanthin	0.0 mcg	
Vitamin C	0.0 mg	0%
Vitamin D	~	~
Vitamin E (Alpha Tocopherol)	0.1 mg	1%
Beta Tocopherol	~	
Gamma Tocopherol	~	
Delta Tocopherol	~	
Vitamin K	4.2 mcg	5%
Thiamin	0.0 mg	0%
Riboflavin	0.0 mg	0%
Niacin	0.0 mg	0%
Vitamin B6	0.0 mg	0%
Folate	0.0 mcg	0%
Food Folate	0.0 mcg	
Folic Acid	0.0 mcg	
Dietary Folate Equivalents	0.0 mcg	
Vitamin B12	0.0 mcg	0%
Pantothenic Acid	0.0 mg	0%
Choline	0.1 mg	
Betaine	0.0 mg	

Minerals

Amounts Per Selected Serving		%DV
Calcium	0.0 mg	0%
Iron	0.0 mg	0%
Magnesium	0.0 mg	0%
Phosphorus	0.0 mg	0%
Potassium	0.0 mg	0%
Sodium	0.0 mg	0%
Zinc	0.0 mg	0%
Copper	0.0 mg	0%
Manganese	~	~
Selenium	0.0 mcg	0%
Fluoride	~	

Sterols

Amounts Per Selected Serving		%DV
Cholesterol	0.0 mg	0%
Phytosterols	49.3 mg	
Campesterol	~	
Stigmasterol	~	
Beta-sitosterol	~	

Other

Amounts Per Selected Serving		%DV
Alcohol	0.0 g	
Water	0.0 g	
Ash	0.0 g	
Caffeine	0.0 mg	
Theobromine	0.0 mg	

Footnotes for Oil, vegetable, walnut

Source. Nutrient data for this listing was provided by USDA SR-21. Each "~" indicates a missing or incomplete value.

Percent Daily Values (%DV) are for adults or children aged 4 or older, and are based on a 2,000 calorie reference diet. Your daily values may be higher or lower based on your individual needs.

Nutrition Data's Opinion, Completeness Score™, Fullness Factor™, Rating, Estimated Glycemic Load (eGL), and Better Choices Substitutions™ are editorial opinions of NutritionData.com, given without warranty, and are not intended to replace the advice of a nutritionist or health-care professional. Nutrition Data's opinions and ratings are based on weighted averages of the nutrient densities of those nutrients for which the FDA has established Daily Values, and do not consider other nutrients that may be important to your health or take into account your individual needs. Consequently, Nutrition Data's higher-rated foods may not necessarily be healthier for you than lower-rated ones. All foods, regardless of their rating, have the potential to play an important role in your diet.

The Amino Acid Score has not been corrected for digestibility, which could reduce its value

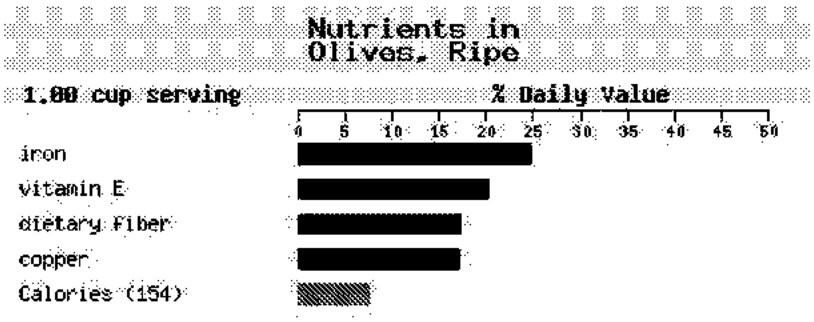
ANNEX D:

Cited art "Olives" and "Olives Nutrient Analysis" from www.whfoods.com webpages http://web.archive.org/web/20060314112112/http://www.whfoods.com/genpage.php?pfriendly=1&tname=foodspice&dbid=46 (published: March 14, 2006) and http://web.archive.org/web/20060314112106/http://www.whfoods.com/genpage.php?tname=nutrientprofile&dbid=111 (published: March14, 2006)

Olives

Sour to bitter, piquant to sweet, the tangy taste of olives are harvested in September but available year round to make a zesty addition to salads, meat and poultry dishes and, of course, pizza.

Olives cannot be eaten right off of the tree; they require special processing to reduce their intrinsic bitterness. These processing methods vary with the olive variety, region where they are cultivated and the desired taste, texture and color. Some olives are picked green and unripe, while others are allowed to fully ripen on the tree to a black color. Yet, not all of the black olives available begin with a black color. Some processing methods expose unripe greens olives to the air, and the subsequent oxidation turns them a dark color. In addition to the original color of the olive, the color is affected by fermentation and/or curing in oil, water, brine or salt.



Health Benefits

Olives are a very good source of monounsaturated fats and a good source of vitamin E. Because monounsaturated fats are less easily damaged than polyunsaturated fats, it's good to have some in our cells' outer membranes and other cell structures that contain fats, such as the membranes that surround the cell's DNA and each of its energy-producing mitochondria. The stability of monounsaturated fats translates into a protective effect on the cell that, especially when combined with the antioxidant protection offered by vitamin E, can lower the risk of damage and inflammation. In addition to vitamin E, olives contain a variety of beneficial active phytonutrient compounds including *polyphenols* and *flavonoids*, that also appear to have significant anti-inflammatory properties.

Cellular Protection Against Free Radicals

Vitamin E is the body's primary fat-soluble antioxidant. It goes after and directly neutralizes free radicals in all the fat-rich areas of the body. In combination, stable monounsaturated fats and vitamin E add a significant safety factor to cellular processes like energy production, a process that generates free radicals even when things are running smoothly.

When cellular processes such as mitochondrial energy production are not well protected, the free radicals produced can interact with and damage any nearby molecules--a process called oxidation. When a cell's mitochondria become damaged, the cell cannot produce enough energy to supply its needs and dies. If a cell's DNA becomes damaged, the cell may mutate and become cancerous.

Protection From Cancer & Heart Disease

Free radical damage can lead to numerous ailments. For example, when free radicals cause the oxidation of cholesterol, the oxidized cholesterol damages blood vessels and builds up in arteries, and can eventually lead to heart attack or stroke. So, by preventing the oxidation of cholesterol, the nutrients in olives help to prevent heart disease.

If free radicals damage the cellular DNA in colon cells, the cells can mutate into cancer cells. By neutralizing free radicals, the nutrients in olives help prevent colon cancer. A higher intake of both vitamin E and the monounsaturated fats in olives is actually associated with lower rates of colon cancer.

Beneficial Anti-Inflammatory Effects

The anti-inflammatory actions of the monounsaturated fats, vitamin E and polyphenols in olives may also help reduce the severity of asthma, osteoarthritis, and rheumatoid arthritis, three conditions where most of the damage is caused by high levels of free radicals. The vitamin E in olives may even help to reduce the frequency and/or intensity of hot flashes in women going through menopause.

Description

Olives are fruits of the tree known as *Olea europaea*. "*Olea*" is the Latin word for "oil," reflecting the olive's very high fat content (15-35%) of which 75% is oleic acid, a monounsaturated fat that has been shown to lower blood cholesterol levels. "Europaea" reminds us that olives are native to the Mediterranean region of Europe.

Olives cannot be eaten right off of the tree; they require special processing to reduce their intrinsic bitterness, caused by the glycoside *oleuropein*, which is concentrated in their skin. These processing methods vary with the olive variety, cultivation region, and the desired taste, texture and color to be created.

Some olives are picked green and unripe, while others are allowed to fully ripen on the tree to a black color. Yet, not all of the black olives available begin with a black color. Some processing methods expose unripe greens olives to the air, and the subsequent oxidation turns them a dark color.

In addition to the original color of the olive determining its finished characteristics, the color is affected by a variety of processing methods that olives undergo including fermentation and/or curing in oil, water, brine or salt. These methods may not only cause the olives to turn black, purple, brown, red, or yellow, but they also affect the skin texture, causing it to be smooth and shiny or wrinkled.

Some of the many available delicious varieties of olives include Moroccan oil-cured,

Kalamata, Nicoise, Picholine and Manzanilla. In addition to varying in size and appearance, the flavor of olives spans the range from sour to smoky to bitter to acidic. In addition to whole olives, you can often find them pitted.

Olive oil is available in a variety of grades that reflects the degree to which it has been processed. Extra-virgin is the initial unrefined oil from the first pressing. Virgin olive oil refers to all oil produced from the first pressing, while pure olive oil usually means a lower-quality oil produced from subsequent pressings. Chemically, the difference bewtween an extra virgin oil and a virgin oil involves the amount of free oleic acid, which is a marker for overall acidity. According to the standards adopted by the International Olive Oil Council, "virgin" can contain up to 2% free oleic acid, while "extra virgin" can contain up to 0.8% of free oleic acid.

History

Olives, one of the oldest foods known, are thought to have originated in Crete between five and seven thousand years ago. Their use quickly spread throughout Egypt, Greece, Palestine and Asia Minor.

Olives are mentioned in the Bible, depicted in ancient Egyptian art, and played an important role in Greek mythology. Since ancient times, the olive tree has provided food, fuel, timber and medicine for many civilizations. It has also been regarded as a symbol of peace and wisdom. Olive oil has been consumed since 3000 BC.

Olives were brought to America by the Spanish and Portuguese explorers during the 15th and 16th century. They were introduced into California by the Franciscan missionaries in the late 18th century. Today, much of the commercial cultivation of olives occurs in Spain, Italy, Greece and Turkey.

How to Select and Store

While olives have been traditionally sold in jars and cans, many stores are now offering them in bulk in large barrels. Buying bulk olives will allow you to experiment with many different types with which you may be unfamiliar and to purchase only as many as you need at one time.

While whole olives are very common, you may also find ones that have been pitted, as well as olives that have been stuffed with either peppers, garlic or almonds. If you purchase olives in bulk, make sure that the store has a good turnover and keeps their olives immersed in brine for freshness and to retain moistness.

Olives will keep freshest if stored in an airtight container in the refrigerator.

How to Enjoy

Tips for Preparing Olives:

To pit olives, press them with the flat side of a broad bladed knife. This will help break the flesh so that you can easily remove the pit with your fingers or the knife. The brine in which olives are packed can be used as a replacement for salted water in recipes.

A Few Quick Serving Ideas:

Olive tapenade is a delicious and easy-to-make spread that you can use as a dip, sandwich spread, or topping for fish and poultry. To make it, put pitted olives in a

food processor with olive oil, garlic, and your favorite seasonings.

Toss pasta with chopped olives, tomatoes, garlic, olive oil and fresh herbs of your choice.

Marinate olives in olive oil, lemon zest, coriander seeds and cumin seeds.

Add chopped olives to your favorite tuna or chicken salad recipe.

Set out a small plate of olives on the dinner table along with some vegetable crudités for your family to enjoy with the meal.

Safety

Olives are not a commonly allergenic food and are not known to contain measurable amounts of goitrogens, oxalates, or purines.

Nutritional Profile

Introduction to Food Rating System Chart

The following chart shows the nutrients for which this food is either an excellent, very good or good source. Next to the nutrient name you will find the following information: the amount of the nutrient that is included in the noted serving of this food; the %Daily Value (DV) that that amount represents (similar to other information presented in the website, this DV is calculated for 25-50 year old healthy woman); the nutrient density rating; and, the food's World's Healthiest Foods Rating. Underneath the chart is a table that summarizes how the ratings were devised. For more detailed information on our **Food and Recipe Rating System**, please click here.

Olives, Ripe 1.00 cup 154.56 calories				
Nutrient	**Amount**	**DV (%)**	**Nutrient Density**	**World's Healthiest Foods Rating**
iron	4.44 mg	24.7	2.9	good
vitamin E	4.03 mg	20.1	2.3	good
dietary fiber	4.30 g	17.2	2.0	good
copper	0.34 mg	17.0	2.0	good

World's Healthiest Foods Rating	**Rule**				
excellent	DV>=75%	OR	Density>=7.6	AND	DV>=10%
very good	DV>=50%	OR	Density>=3.4	AND	DV>=5%
good	DV>=25%	OR	Density>=1.5	AND	DV>=2.5%

References

- Aguilera CM, Ramirez-Tortosa MC, Mesa MD, Gil A. [Protective effect of monounsaturated and polyunsaturated fatty acids on the development of cardiovascular disease]. Nutr Hosp 2001 May-2001 Jun 30;16(3):78-91.
- Bond R, Lloyd DH. A double-blind comparison of olive oil and a combination of evening primrose oil and fish oil in the management of canine atopy. Vet Rec 1992 Dec 12;131(24):558-60.
- Ensminger AH, Ensminger, ME, Kondale JE, Robson JRK. Foods & Nutriton Encyclopedia. Pegus Press, Clovis, California.
- Ensminger AH, Esminger M. K. J. e. al. Food for Health: A Nutrition Encyclopedia. Clovis, California: Pegus Press; 1986.
- Fortin, Francois, Editorial Director. The Visual Foods Encyclopedia. Macmillan, New York.
- Martinez-Dominguez E, de la Puerta R, Ruiz-Gutierrez V. Protective effects upon experimental inflammation models of a polyphenol-supplemented virgin olive oil diet. Inflamm Res 2001 Feb;50(2):102-6.
- Martinez-Dominguez E, de la Puerta R, Ruiz-Gutierrez V. Protective effects upon experimental inflammation models of a polyphenol-supplemented virgin olive oil diet. Inflamm Res 2001; 50(2): 102-6.
- Owen RW, Haubner R, Mier W et al. Isolation, structure elucidation and antioxidant potential of the major phenolic and flavonoid compounds in brined olive drupes. Food Chem Toxicol 2003 May; 41(5):703-17.
- Visioli F, Romani A, Mulinacci N, et al. Antioxidant and other biological activities of olive mill waste waters. J Agric Food Chem 1999 Aug;47(8):3397-401.
- Wood, Rebecca. The Whole Foods Encyclopedia. New York, NY: Prentice-Hall Press; 1988.

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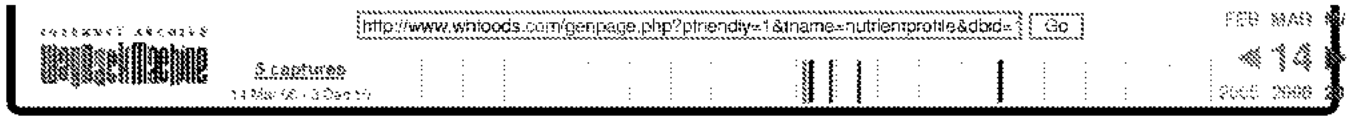
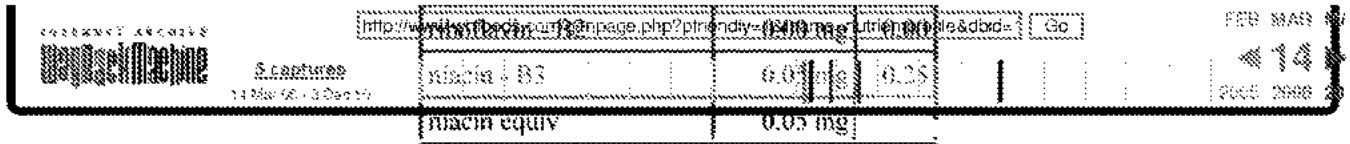


The World's Healthiest Foods

Olives, Ripe

In depth nutrient analysis:

Olives, Ripe		
amount	1.00 cup	
total weight	134.40 g	
Basic Components		
nutrient	**amount**	**%DV**
calories	154.56	
calories from fat	129.19	
calories from saturated fat	17.12	
protein	1.13 g	
carbohydrates	8.41 g	
dietary fiber	4.30 g	17.20
soluble fiber	0.22 g	
insoluble fiber	4.09 g	
sugar - total	4.11 g	
monosaccharides	-- g	
disaccharides	-- g	
other carbs	0.00 g	
fat - total	14.35 g	
saturated fat	1.90 g	
mono fat	10.60 g	
poly fat	1.22 g	
trans fatty acids	0.00 g	
cholesterol	0.00 mg	
water	107.51 g	
ash	3.00 g	
Vitamins		
nutrient	**amount**	**%DV**
vitamin A IU	541.63 IU	10.83
vitamin A RE	53.76 RE	
A - carotenoid	53.76 RE	0.72
A - retinol	0.00 RE	
A - beta carotene	-- mcg	
thiamin - B1	0.00 mg	0.00



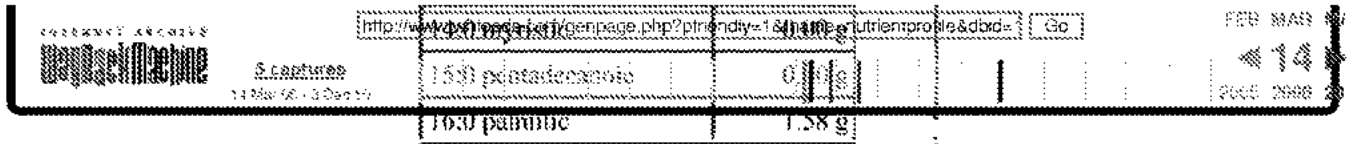
riboflavin B2	0.03 mg	1.76
niacin B3	0.63 mg	3.15
niacin equiv	0.65 mg	
vitamin B6	0.01 mg	0.50
vitamin B12	0.00 mcg	0.00
biotin	-- mcg	--
vitamin C	1.21 mg	2.02
vitamin D IU	0.00 IU	0.00
vitamin D mcg	0.00 mcg	
vitamin E alpha equiv	4.03 mg	20.15
vitamin E IU	6.01 IU	
vitamin E mg	4.03 mg	
folate	0.00 mcg	0.00
vitamin K	-- mcg	--
pantothenic acid	0.02 mg	0.20

Minerals

nutrient	amount	%DV
boron	-- mcg	
calcium	118.27 mg	11.83
chloride	-- mg	
chromium	-- mcg	--
copper	0.34 mg	17.00
fluoride	-- mg	--
iodine	-- mcg	--
iron	4.44 mg	24.67
magnesium	5.38 mg	1.34
manganese	0.03 mg	1.50
molybdenum	-- mcg	--
phosphorus	4.03 mg	0.40
potassium	10.75 mg	
selenium	1.21 mcg	1.73
sodium	1171.97 mg	
zinc	0.30 mg	2.00

Saturated Fats

nutrient	amount	%DV
4:0 butyric	0.00 g	
6:0 caproic	0.00 g	
8:0 caprylic	0.00 g	
10:0 capric	0.00 g	
12:0 lauric	0.00 g	



14:0 myristic	0.08 g
15:0 pentadecenoic	0.00 g
16:0 palmitic	1.58 g
17:0 margaric	0.00 g
18:0 stearic	0.32 g
20:0 arachidic	0.00 g
22:0 behenate	0.00 g
24:0 lignoceric	0.00 g

Mono Fats

nutrient	amount	%DV
14:1 myristol	0.00 g	
15:1 pentadecenoic	0.00 g	
16:1 palmitol	0.12 g	
17:1 heptadecenoic	0.00 g	
18:1 oleic	10.44 g	
20:1 eicosen	0.04 g	
22:1 erucic	0.00 g	
24:1 nervonic	0.00 g	

Poly Fats

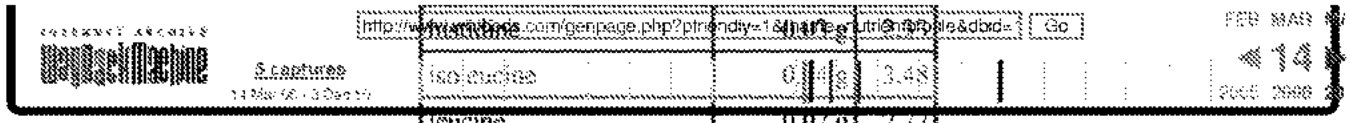
nutrient	amount	%DV
18:2 linoleic	1.14 g	
18:3 linolenic	0.09 g	
18:4 stearidon	0.00 g	
20:3 eicosatrienoic	0.00 g	
20:4 arachidon	0.00 g	
20:5 EPA	0.00 g	
22:5 DPA	0.00 g	
22:6 DHA	0.00 g	

Other Fats

nutrient	amount	%DV
omega 3 fatty acids	0.09 g	3.60
omega 6 fatty acids	1.14 g	

Amino Acids

nutrient	amount	%DV
alanine	0.06 g	
arginine	0.09 g	
aspartate	0.12 g	
cystine	0.00 g	0.00
glutamate	0.12 g	
glycine	0.07 g	



isoleucine	0 g	3.48
leucine	0.07 g	2.77
lysine	0.04 g	1.70
methionine	0.02 g	2.70
phenylalanine	0.04 g	3.36
proline	0.05 g	
serine	0.04 g	
threonine	0.03 g	2.42
tryptophan	0.00 g	0.00
tyrosine	0.03 g	3.09
valine	0.05 g	3.40

Other

nutrient	amount	%DV
alcohol	0.00 g	
caffeine	0.00 mg	
artif sweetener total	-- mg	
aspartame	-- mg	
saccharin	-- mg	
sugar alcohol	-- g	
glycerol	-- g	
inositol	-- g	
mannitol	-- g	
sorbitol	-- g	
xylitol	-- g	
organic acids	-- mg	
acetic acid	-- mg	
citric acid	-- mg	
lactic acid	-- mg	
malic acid	-- mg	
choline	-- mg	--
taurine	-- mg	

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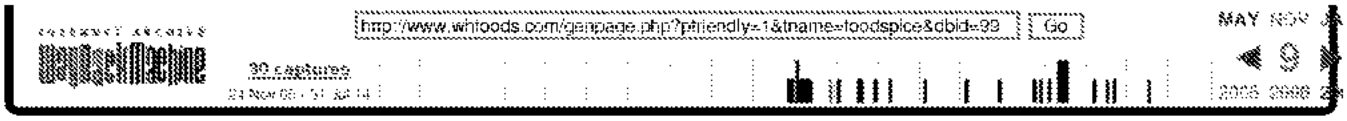
ANNEX E:

Cited art "Walnuts" and "Walnut Nutrient Analysis" from www.whfoods.com webpages http://web.archive.org/web/20061109210019/http://www.whfoods.com/genpage.php?tname=foodspice&dbid=99 (published: November 9, 2006) and http://web.archive.org/web/20061109221127/http://www.whfoods.com/genpage.php?tname=nutrientprofile&dbid=132 (published: November 9, 2006)



The World's Healthiest Foods

Walnuts are a delicious way to add extra nutrition, flavor and crunch to a meal. While walnuts are harvested in December, they are available year round a great source of those all-important omega-3 fatty acids.

It is no surprise that the regal and delicious walnut comes from an ornamental tree that is highly prized for its beauty. The walnut kernel consists of two bumpy lobes that look like abstract butterflies. The lobes are off white in color and covered by a thin, light brown skin. They are partially attached to each other. The kernels are enclosed in round or oblong shells that are brown in color and very hard.

Food Chart

Health Benefits

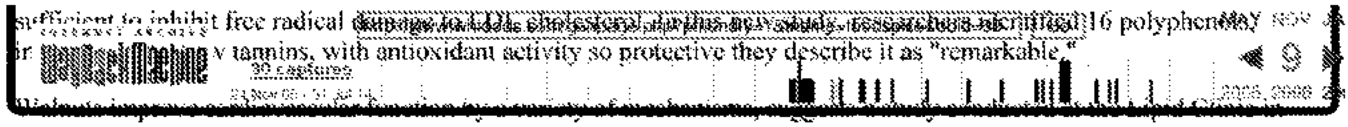
When it comes to their health benefits, walnuts definitely are not a hard nut to crack. This delicious nut is an excellent source of omega-3 essential fatty acids, a special type of protective fat the body cannot manufacture. Walnuts' concentration of omega-3s (a quarter-cup provides 90.8% of the daily value for these essential fats) has many potential health benefits ranging from cardiovascular protection, to the promotion of better cognitive function, to anti-inflammatory benefits helpful in asthma, rheumatoid arthritis, and inflammatory skin diseases such as eczema and psoriasis. In addition, walnuts contain an antioxidant compound called *ellagic acid* that supports the immune system and appears to have several anticancer properties.

Take Walnuts to Heart

Adding walnuts to your diet can be an important step in improving your cardiovascular health. Walnuts are an important source of monounsaturated fats—approximately 15% of the fat found in walnuts is healthful monounsaturated fat. A host of studies have shown that increasing the dietary intake of monounsaturated-dense walnuts has favorable effects on high cholesterol levels and other cardiovascular risk factors. One particular study compared the effects of a cholesterol-lowering Mediterranean diet with an adjusted Mediterranean diet in which 35% of the calories derived from monounsaturated fats came from walnuts. When following the walnut-rich diet, the 49 study participants were found to have lower levels of total cholesterol, LDL (the dangerous form) cholesterol and Lp(a) ("lipoprotein a," another lipid compound that increases blood clotting and, when elevated, is considered a risk factor for atherosclerosis).

In addition to their heart-protective monounsaturated fats, walnuts' concentration of omega-3 essential fatty acids is also responsible for the favorable effects walnut consumption produces on cardiovascular risk factors. Omega-3s benefit the cardiovascular system by helping to prevent erratic heart rhythms, making blood less likely to clot inside arteries (which is the proximate cause of most heart attacks), and improving the ratio of good (HDL) cholesterol to potentially harmful (LDL) cholesterol. Omega-3s also reduce inflammation, which is a key component in the processes that turn cholesterol into artery-clogging plaques.

Since walnuts contain relatively high levels of *l-arginine*, an essential amino acid, they may also be of special import when it comes to hypertension. In the body (specifically within those hard-working blood vessels), l-arginine is converted into *nitric oxide*, a chemical that helps keep the inner walls of blood vessels smooth and allows blood vessels to relax. Since individuals with hypertension have a harder time maintaining normal nitric oxide levels, which may also relate to other significant health issues such as diabetes and heart problems, walnuts can serve as a great addition to their diets. A study published in *Phytochemistry* sheds further light on walnuts' cardioprotective benefits. Earlier research had already suggested that several polyphenolic compounds found in walnuts, specifically ellagic and gallic acid, possessed antioxidant activity



Barcelona, Spain, and published in *Circulation*.

For four weeks, 21 men and women with high cholesterol followed either a regular, low-caloric Mediterranean diet or one in which walnuts were substituted for about one-third of the calories supplied by olives, olive and other monounsaturated fats in the Mediterranean diet. Then, for a second four weeks, they switched over to the diet they had not yet been on.

Not only did the walnut diet significantly reduce total cholesterol (a drop that ranged from 4.4 to 7.4%) and LDL (bad) cholesterol (a drop ranging from 6.4 to 10%), but walnuts were also found to increase the elasticity of the arteries by 64%, and to reduce levels of vascular cell adhesion molecules, a key player in the development of atherosclerosis (hardening of the arteries).

The researchers found that the drop in cholesterol correlated with increases in blood levels of alpha-linolenic acid, a key essential fatty acid from which long chain omega-3 fats (such as EPA) can be derived, and gamma-tocopherol, a form of vitamin E. Walnuts are uniquely rich in both of these nutrients, which have shown heart protective benefits in other studies.

The U.S. Food and Drug Administration has recently cleared the health claim that "eating 1.5 ounces per day of walnuts as part of a diet low in saturated fat and cholesterol may reduce the risk of heart disease." "This is the first time a whole food, not its isolated components, has shown this beneficial effect on vascular health," said Emilio Ros, who led the study at the Hospital Clinic of Barcelona.

Walnuts Improve Cholesterol Profile in Persons with Type 2 Diabetes

In patients with type 2 diabetes, including a daily ounce of walnuts in a diet in which 30% of calories came from fat translated into a significant improvement in subjects' cholesterol profile.

In this study, published in *Diabetes Care*, 58 men and women with an average age of 59 years, were assigned to one of three diets in which 30% of calories was derived from fat: a low fat diet, a modified low fat diet, and a modified low fat diet including an ounce of walnuts per day.

After 6 months, those on the walnut diet had achieved a significantly greater increase in their HDL-to-total cholesterol ratio than the other groups, plus walnut eaters saw a 10% reduction in their LDL cholesterol. Why such benefit from walnuts? Most likely because walnuts are exceptionally high in their content of monounsaturated fat and the omega-3 fatty acid, alpha-linolenic acid. Plus, walnuts combine these heart healthy fats with a hefty dose of the antioxidants including at least 16 antioxidant phenols, vitamin E, ellagic and gallic acid.

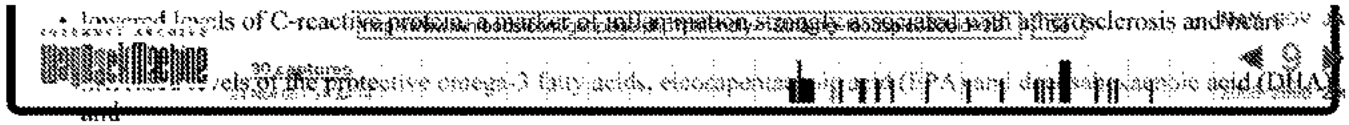
Additional research has confirmed that when walnuts are eaten as part of a modified low-fat diet, the result is a more cardiprotective fat profile in diabetic patients than can be achieved by simply lowering the fat content of the diet. In a study published in the *Journal of the American Dietetic Association*, all 55 study participants with type 2 diabetes were put on low fat diets, but the only group to achieve a cardioprotective fat profile (less than 10% of calories from saturated fat, 7-10% of calories from polyunsaturated fats, adequate omega-3 fats, and an omega-6:omega-3 ratio of less than 10) were those who ate walnuts (30 grams—about one ounce—per day).

Walnuts Found to Reduce Levels of Several Molecules that Promote Atherosclerosis

In addition to walnuts' beneficial effects on cholesterol, more insight into the reasons why walnuts reduce the risk of coronary heart disease were revealed in research published in the *Journal of Nutrition*.

The study involved 20 overweight or obese men, 30 to 60 years old, and 3 menopausal women, aged 55-65, all of whom had elevated LDL cholesterol levels. Each subject was assigned to one of the three diets on a rotating six-week basis with a two-week break between each one. The average American diet served as the control diet, while the two experimental diets were a linoleic acid (LA) diet that included an ounce of walnuts and a teaspoon of walnut oil daily, and an alpha-linoleic acid diet (ALA), which added a teaspoon of flaxseed oil, which is especially high in ALA, to the linoleic diet.

Both experimental diets resulted in positive effects, with the ALA diet providing the most benefit. In addition to lowering LDL cholesterol, the walnut-rich ALA diet:



- decreased levels of ICAM-1 and VCAM-1 and E-selection, all of which are involved in cholesterol's adhesion to the endothelium (the lining of the arteries).

Food for Better Thought

Walnuts have often been thought of as a "brain food," not only because of the wrinkled brain-like appearance of their shells, but because of their high concentration of omega-3 fats. Your brain is more than 60% structural fat. For your brain cells to function properly, this structural fat needs to be primarily the omega-3 fats found in walnuts, flaxseed and cold-water fish. This is because the membranes of all our cells, including our brain cells or *neurons*, are primarily composed of fats. Cell membranes are the gatekeepers of the cell. Anything that wants to get into or out of a cell must pass through the cell's outer membrane. And omega-3 fats, which are especially fluid and flexible, make this process a whole lot easier, thus maximizing the cell's ability to usher in nutrients while eliminating wastes--definitely a good idea, especially when the cell in question is in your brain.

Epidemiological studies in various countries including the U.S. suggest a connection between increased rates of depression and decreased omega-3 consumption, and in children, the relationship between low dietary intake of omega-3 fats and ADHD has begun to be studied. A recent Purdue University study showed that kids low in omega-3 essential fatty acids are significantly more likely to be hyperactive, have learning disorders, and to display behavioral problems. In the Purdue study, a greater number of behavioral problems, temper tantrums, and sleep problems were reported in subjects with lower total omega-3 fatty acid concentrations. More learning and health problems were also found in the children in the study who had lower total omega-3 fatty acid concentrations.

Over 2,000 scientific studies have demonstrated the wide range of problems associated with omega-3 deficiencies. The American diet is almost devoid of omega-3s, except for nuts, such as walnuts, seeds and cold-water fish. In fact, researchers believe that about 60% of Americans are deficient in omega-3 fatty acids, and about 20% have so little that test methods cannot even detect any in their blood.

Help Prevent Gallstones

Twenty years of dietary data collected on over 80,000 women from the Nurses' Health Study shows that women who eat least 1 ounce of nuts, peanuts or peanut butter each week have a 25% lower risk of developing gallstones. Since 1 ounce is only 28.6 nuts or about 2 tablespoons of nut butter, preventing gallbladder disease may be as easy as having a handful of walnuts as an afternoon pick me up, or tossing some walnuts on your oatmeal or salad.

A Source of Bio-Available Melatonin

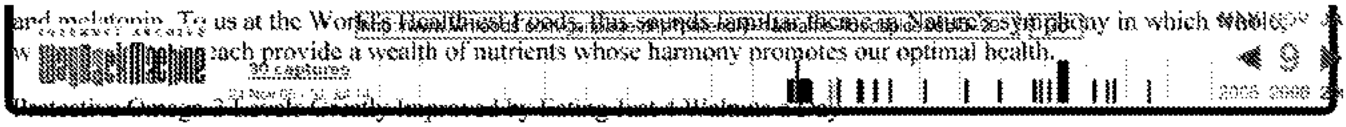
Want a better night's sleep? Try sprinkling your dinner's tossed green salad, fruit salad or steamed vegetables with a handful of walnuts. Or enjoy a baked apple or poached pear topped with walnuts for dessert.

Melatonin, a hormone produced by the pineal gland, which is involved in inducing and regulating sleep and is also a powerful antioxidant, has been discovered in walnuts in bio-available form, making them the perfect evening food for a natural good night's sleep.

Melatonin has been shown to help improve sleep for night shift workers and people suffering from jet lag, but maintaining healthy levels of this hormone is important for everyone over the age of 40 since the amount of melatonin produced by the human body decreases significantly as we age, and this decrease in antioxidant protection may be related to the development of free radical-related diseases later in life.

In a study published in *Nutrition*, Russell Reiter and colleagues at the University of Texas have not only quantified the amount of melatonin present in walnuts-between 2.5 and 4.5 ng/gram-but have demonstrated that eating walnuts triples blood levels of melatonin and also increases antioxidant activity in the bloodstream in animals.

The authors theorize that by helping the body resist oxidative stress (free radical damage), walnuts may help reduce the risk of cancer and delay or reduce the severity of cardiovascular disease and neurodegenerative diseases such as Parkinson's or Alzheimer's disease. Walnuts, best known as a heart-healthy nut, are also a rich source of another highly cardio-protective nutrient: omega-3-fatty acids, so Reiter and his team will next investigate possible synergy between walnuts' omega-3 fats



Enjoying just 4 walnuts a day significantly increased blood levels of the health-protective omega-3 essential fatty acids, alpha linolenic acid (ALA) and eicosapentaenoic acid (EPA), in 10 adults.

EPA, a longer-chain omega-3 fat, is already present in cold water fish, but is not found in nuts, which contain the shorter-chain omega-3 fat, ALA. Fortunately, as this study confirms, our bodies can make EPA from the ALA provided by walnuts, which are its richest source among all the nuts.

After a 2-week run-in period, during which no walnuts were eaten, blood levels of ALA and EPA were assessed, and study participants then ate 4 walnuts a day, in addition to their regular diet, for 3 weeks.

When blood tests were again run, significant increases in levels of ALA (from 0.23 to 0.47) and EPA (from 0.23 to 0.82) were seen. And levels of ALA and EPA remained elevated over subjects' initial levels even after a final 2-week period during which no walnuts were eaten. This study, published in *Nutrition, Metabolism and Cardiovascular Diseases*, clearly shows that even a very simple change in diet can have highly beneficial and lasting effects on our health. Boosting your body's supply of cardio-protective, anti-inflammatory omega-3 fatty acids couldn't be any easier-just add a few walnuts to your morning cereal or daily salad or just grab a handful for an afternoon snack.

That's Nut the End of Walnut's Health Benefits

Walnuts are a very good source of manganese and a good source of copper, two minerals that are essential cofactors in a number of enzymes important in antioxidant defenses. For example, the key oxidative enzyme *superoxide dismutase*, which disarms free radicals produced within cell cytoplasm and the mitochondria (the energy production factories within our cells) requires both copper and manganese.

Walnuts also contain an antioxidant compound called *ellagic acid*, which blocks the metabolic pathways that can lead to cancer. Ellagic acid not only helps protect healthy cells from free radical damage, but also helps detoxify potential cancer-causing substances and helps prevent cancer cells from replicating. In a study of over 1,200 elderly people, those who ate the most strawberries (another food that contains ellagic acid) were three times less likely to develop cancer than those who ate few or no strawberries.

Description

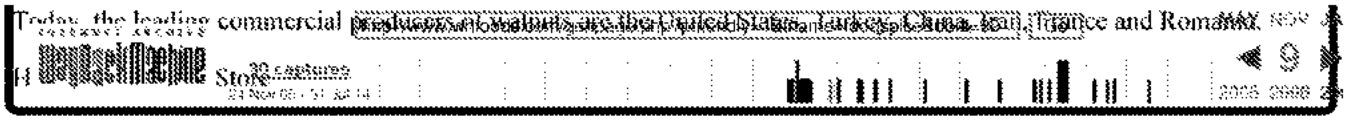
It is no surprise that the regal and delicious walnut comes from an ornamental tree that is highly prized for its beauty. The walnut kernel consists of two bumpy lobes that look like abstract butterflies. The lobes are off white in color and covered by a thin, light brown skin. They are partially attached to each other. The kernels are enclosed in round or oblong shells that are brown in color and very hard.

While there are numerous species of walnut trees, three of the main types of walnuts consumed are the English (or Persian) walnut, *Juglans regia*; the Black walnut, *Juglans nigra*; and the White (or butternut) walnut, *Juglans cinerea*. The English walnut is the most popular type in the United States and features a thinner shell that is easily broken with a nutcracker. The Black walnut has thicker shells that are harder to crack and a much more pungent distinctive flavor. The White walnut features a sweeter and oilier taste than the other two types, although it is not as widely available and therefore may be more difficult to find in the marketplace.

History

While walnut trees have been cultivated for thousands of years, the different types have varying origins. The English walnut originated in India and the regions surrounding the Caspian Sea, hence it is known as the Persian walnut. In the 4th century AD, the ancient Romans introduced the walnut into many European countries where it has been grown since. Throughout its history, the walnut tree has been highly revered; not only does it have a life span that is several times that of humans, but its uses include food, medicine, shelter, dye and lamp oil. It is thought that the walnuts grown in North America gained the moniker "English walnuts," since they were introduced into America via English merchant ships.

Black walnuts and white walnuts are native to North America, specifically the Central Mississippi Valley and Appalachian area. They played an important role in the diets and lifestyles of both the Native American Indians and the early colonial settlers.



When purchasing whole walnuts that have not been shelled, choose those that feel heavy for their size. Their shells should not be cracked, pierced or stained, as this is oftentimes a sign of mold development on the nutmeat, which renders it unsafe for consumption.

Shelled walnuts are generally available in prepackaged containers as well as bulk bins. Just as with any other food that you may purchase in the bulk section, make sure that the bins containing the walnuts are covered and that the store has a good product turnover so as to ensure its maximal freshness. Whether purchasing walnuts in bulk or in a packaged container, avoid those that look rubbery or shriveled. If it is possible to smell the walnuts, do so in order to ensure that they are not rancid.

Due to their high polyunsaturated fat content, walnuts are extremely perishable and care should be taken in their storage. Shelled walnuts should be stored in an airtight container and placed in the refrigerator, where they will keep for six months, or the freezer, where they will last for one year. Unshelled walnuts should preferably be stored in the refrigerator, although as long as you keep them in a cool, dry, dark place they will stay fresh for up to six months.

How to Enjoy

For some of our favorite recipes, click Recipes.

A Few Quick Serving Ideas:

Mix crushed walnuts into plain yogurt and top with maple syrup.

Add walnuts to healthy sautéed vegetables.

Walnuts are great in baked goods and breakfast treats. Some of our favorites include zucchini walnut bread, carrot walnut muffins and apple walnut pancakes.

Purée walnuts, cooked lentils and your favorite herbs and spices in a food processor. Add enough olive or flax oil so that it achieves a dip-like consistency.

Sprinkle walnuts onto salads.

Add walnuts to your favorite poultry stuffing recipe.

To roast walnuts at home, do so gently—in a 160-170°F (about 75°C) oven for 15-20 minutes—to preserve the healthy oils. For more on the effect of high heat roasting on nuts, please see the following article.

Make homemade walnut granola: Mix together aproximately 1/2 cup of honey, 3 to 4 tablespoons of blackstrap molasses, a tablespoon of vanilla, a dash of salt, and a teaspoon each of your favorite spices, such as cinnamon, ginger and/or nutmeg. Place 6-8 cups of rolled oats in a large bowl and toss to coat with the honey-blackstrap mixture. Then spread on a cookie sheet and bake at 275°F(135°C) for 45 minutes. Cool and mix in 1/2 to 1 cup of walnuts.

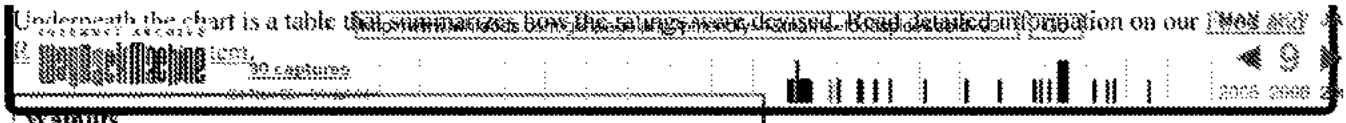
Safety

Walnuts are not a commonly allergenic food and are not known to contain measurable amounts of goitrogens, oxalates, or purines.

Nutritional Profile

Introduction to Food Rating System Chart

The following chart shows the nutrients for which this food is either an excellent, very good or good source. Next to the nutrient name you will find the following information: the amount of the nutrient that is included in the noted serving of this food; the %Daily Value (DV) that that amount represents (similar to other information presented in the website, this DV is calculated for 25-50 year old healthy woman); the nutrient density rating; and, the food's World's Healthiest Foods Rating.



Walnuts **0.25 cup** **163.50 calories**				
Nutrient	**Amount**	**DV (%)**	**Nutrient Density**	**World's Healthiest Foods Rating**
omega 3 fatty acids	2.27 g	90.8	10.0	excellent
manganese	0.85 mg	42.5	4.7	very good
copper	0.40 mg	20.0	2.2	good
tryptophan	0.05 g	15.6	1.7	good

World's Healthiest Foods Rating	**Rule**				
excellent	DV>=75%	OR	Density>=7.6	AND	DV>=10%
very good	DV>=50%	OR	Density>=3.4	AND	DV>=5%
good	DV>=25%	OR	Density>=1.5	AND	DV>=2.5%

References

- Anderson K.J.; Teuber S.S.; Gobeille A.; Cremin P.; Waterhouse A.L.; Steinberg F.M. Walnut polyphenolics inhibit in vitro human plasma and LDL oxidation. *Journal of Nutrition*, Vol. 131, Issue 11: 2837-2842 2001
- Ensminger AH, Ensminger, ME, Kondale JE, Robson JRK. Foods & Nutriton Encyclopedia. Pegus Press, Clovis, California 1983
- Ensminger AH, Esminger M. K. J. e. al. Food for Health: A Nutrition Encyclopedia. Clovis, California: Pegus Press; 1986. PMID: 15210
- Fortin, Francois, Editorial Director. The Visual Foods Encyclopedia. Macmillan, New York 1996
- Fukuda T, Ito H, Yoshida T. Antioxidative polyphenols from walnuts (*Juglans regia L.*). *Phytochemistry*. Aug;63 (7):795-801 2003
- Gillen LJ, Tapsell LC, Patch CS, Owen A, Batterham M. Structured dietary advice incorporating walnuts achieves optimal fat and energy balance in patients with type 2 diabetes mellitus. *J Am Diet Assoc*. 2005 Jul;105(7):1087-96., PMID: 15983525
- Marangoni F, Colombo C, Martiello A, Poli A, Paoletti R, Galli C. Levels of the n-3 fatty acid eicosapentaenoic acid in addition to those of alpha linolenic acid are significantly raised in blood lipids by the intake of four walnuts a day in humans. *Nutr Metab Cardiovasc Dis*. 2006 Sep 25; [Epub ahead of print] . PMID: 17008073
- Morgan JM, Horton K, Reese D et al. Effects of walnut consumption as part of a low-fat, low-cholesterol diet on serum cardiovascular risk factors. Int J Vitam Nutr Res 2002 Oct; 72(5):341-7 2002
- Patel G. Essential fats in walnuts are good for the heart and diabetes. *J Am Diet Assoc*. 2005 Jul;105(7):1096-7., PMID: 15983525
- Reiter RJ, Manchester LC, Tan DX. Melatonin in walnuts: influence on levels of melatonin and total antioxidant capacity of blood. *Nutrition*. 2005 Sep;21(9):920-4. , PMID: 15979282
- Ros E, Nunez I, Perez-Heras A, Serra M, Gilabert R, Casals E, Deulofeu R. A walnut diet improves endothelial function in hypercholesterolemic subjects: a randomized crossover trial. *Circulation*. 2004 Apr 6;109(13):1609-14. , PMID: 15037535
- Stevens LJ, Zentall SS, Abate ML, et al. Omega-3 Fatty Acids in Boys with Behavior, Learning, and Health Problems. Physiol Behav 59(4/5) 915-920. 1996 1996
- Stevens LJ, Zentall SS, Deck JL, et al. Essential Fatty Acid Metabolism in Boys with Attention-Deficit Hyperactivity Disorder. American Journal of Clinical Nutrition, 1995 Oct; 62(4): 761-8 1995
- Tapsell LC, Gillen LJ, Patch CS, Batterham M, Owen A, Bare M, Kennedy M. Including Walnuts in a Low-Fat/Modified-Fat Diet Improves HDL Cholesterol-to-Total Cholesterol Ratios in Patients With Type 2 Diabetes. *Diabetes Care*. 2004 Dec;27(12):2777-83., PMID: 15562184
- Tsai CJ, Leitzmann MF, Hu FB, Willett WC, Giovannucci EL. . Frequent nut consumption and decreased risk of cholecystectomy in women. *Am J Clin Nutr*. 2004 Jul;80(1):76-81., PMID: 15213031
- Wood, Rebecca. The Whole Foods Encyclopedia. New York, NY: Prentice-Hall Press; 1988. PMID: 15220

Zhao G, Etherton TD, Martin KR, West SG, Gillies PJ, Kris-Etherton PM. Dietary Alpha-Linolenic Acid Reduces Inflammatory and Lipid Cardiovascular Risk Factors in Hypercholesterolemic Men and Women. *J Nutr*. 2004; 9 PMID: 15514264

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George Mateljan Foundation

Walnuts

In depth nutrient analysis:

Walnuts +Qrwh=#0\&lgglfdwhv#gdwd#lv#**unavailable**,		
dprxqw	3158#fxs	
wrwdo#zhljkw	58133#j	
Basic Components		
nutrient	**amount**	**% DV**
fdorulhv	496183	
fdorulhv#iurp#idw	4791:5	
fdorulhv#iurp#vdwxudwhg#idw	461:;	
surwhlq	61;4#j	
fduerk|gudwhv	6176#j	
glhwdu|#iledu	419;#j	91:5
vroxeoh#iledu	3173#j	
lqvroxeoh#iledu	31;4#j	
vxjdu#0#wrwdo	3199#j	
prqrvdffkdulghv	3133#j	
glvdffkdulghv	3186#j	
rwkhu#fduev	4143#j	
idw#0#wrwdo	49163#j	
vdwxudwhg#idw	4186#j	
prqr#idw	5156#j	
sro|#idw	441:<#j	
wudqv#idw|#dflgv	3133#j	
fkrohvwhuro	3133#pj	
zdwhu	4135#j	
dvk	3179#j	
Vitamins		
nutrient	**amount**	**% DV**
ylwdplq#D#LX	43153#LX	3153
ylwdplq#D#UH	4133#UH	
D#0#fduwhqrlg	4133#UH	3134
D#0#uhwlqro	3133#UH	
D#0#ehwd#fdurwhqh	9133#pfj	
wkldplq#0#E4	313<#pj	9133
uleriodylq#0#E5	3137#pj	5168
qldflq#0#E6	317;#pj	5173
qldflq#htxly	4156#pj	
yLwdplq#E9	3146#pj	9193
yLwdplq#E45	3133#pfj	3133
elrwlq	71:5#pfj	418;

ylwdp lq#F	3166#p j	3198
ylwdp lq#G#LX	3133#LX	3133
ylwdp lq#G#p fj	3133#p fj	
ylwdp lq#H#dopk d#wtxly	31:7#p j	61:3
ylwdp lq#H#LX	4143#LX	
ylwdp lq#H#p j	31:7#p j	
iroiwh	57183#p fj	9146
ylwdp lq#N	319;#p fj	31;8
sdqwrwkhqlf#dflg	3147#p j	4173

Minerals

nutrient	amount	% DV
erurq	00#p fj	
fdofxp	59133#p j	5193
fkoruljh	9133#p j	
fkurp lxp	00#p fj	00
frsshu	3173#p j	53133
ioxrulgh	00#p j	00
lrglgh	5153#p fj	4133
lurq	31:6#p j	7139
p djqhvlxp	6<183#p j	<1;;
p dqjdqhvh	31;8#p j	75183
p roteghqxp	:16;#p fj	<1;7
skrvskruxv	;9183#p j	;198
srwdvvlxp	443158#p j	
vhohqlxp	4143#p fj	4197
vrglxp	3183#p j	
}lqf	31::#p j	8146

Saturated Fats

nutrient	amount	% DV
7=3#exw|ulf	3133#j	
9=3#Fdsurlf	3133#j	
;=3#Fdsu|olf	3133#j	
43=3#Fdsulf	3133#j	
45=3#odxulf	3133#j	
47=3#p |ulvwlf	3133#j	
48=3#shqwdghfdqrlf	3133#j	
49=3#sdop lwlf	4143#j	
4:=3#p dujdulf	3133#j	
4;=3#vwhdulf	3174#j	
53=3#dudfklglf	3135#j	
55=3#ehkhqdwh	3133#j	
57=3#oljqrfhulf	3133#j	

Mono Fats

nutrient	amount	% DV
47=4#p |ulvwro	3133#j	
48=4#shqwdghfhqrlf	3133#j	
49=4#sdop lwro	3133#j	
4:=4#khswdghfhqrlf	3133#j	
4;=4#rdnlf	5153#j	
53=4#hlfrvhq	3136#j	
55=4#hux flf	3133#j	
57=4#[illegible]		

	3133#j	

Poly Fats

nutrient	amount	% DV
4;=5#dqrdlf	<185#j	
4;=6#1lqrdwqlf	515:#j	
4;=7#vwhdulgrq	3133#j	
53=6#hlfrvdwulhqrlf	3133#j	
53=7#dudfklgrq	3133#j	
53=8#HSD	3133#j	
55=0#GSD	3133#j	
55=9#GKD	3133#j	

Other Fats

nutrient	amount	% DV
rphjd#6#idww|#dflgv	515:#j	<31;3
rphjd#9#idww|#dflgv	<185#j	

Amino Acids

nutrient	amount	% DV
dodqlqh	314:#j	
dujlqlqh	3189#j	
dvsduwdwh	3177#j	
f|vwlqh	3138#j	45153
joxwdpdwh	319;#j	
jo|flqh	3153#j	
klvwlglqh	313<#j	9:<;
lvrohxflqh	3148#j	46137
ohxflqh	315;#j	44413;
o|vlqh	3143#j	7159
phwklrqlqh	3139#j	;144
skhq|ododqlqh	314:#j	4715<
surolqh	314:#j	
vhulqh	3156#j	
wkuhrqlqh	3147#j	4415<
wu|swrskdq	3138#j	48196
w|urvlqh	3143#j	43164
ydolqh	314;#j	45157

Other

nutrient	amount	% DV
dofrkro	3133#j	
fdiihlqh	3133#pj	
duwliflfldo#vzhhwhqhu#wrwdo	00pj	
dvsduwdph	00pj	
vdffkdulq	00pj	
vxjdu#dofrkro	00j	
jo|fhuro	00j	
lqrvlwro	00j	
pdqqlwro	00j	
vruelwro	00j	
{|olwro	00j	
rujdqlf#dflgv	00pj	
dfhwlf#dflg	00pj	
flwulf#dflg	00pj	
[illegible]		

	00 p j	
p dqf#dflg	00 p j	
fkrdgh	00 p j	00
wdxulqh	00 p j	

Note: #Wkh#qxwulhqw#surilohv#surylghg#lq#wklv#zhevlwh#duh#ghulyhg#iurp#Irrg#Surfhvvru#iru#Z lqgrzv/#Yhuvlrq#:193/#e|#4 HVKD#Uhvhdufk#lq#Vdohp/#Rujhrq/#XVD1#Ri#wkh#54/95<#irrg#uhfrugv#frqwdlqhg#lq#wkh#HVKD#irrgv#gdwdedvh/#prvw#ri# wkhp#0#lqfoxglqj#wkrvh#ri#wkh#Zruog*v#Khdowklhvw#Irrgv#0#odfnhg#lqirupdwlrq#iru#vshflilf#qxwulhqw1#Wkh#ghvljqdwlrq#%00 %#zdv#fkrvhq#wr#uhsuhvhqw#wkrvh#qxwulhqwv#iru#zklfk#wkhuh#zdv#qr#phdvxuhphqw#lqfoxghg#lq#wkh#HVKD#irrgv# gdwdedvh1#

ANNEX F:

Mark et al., U.S. Patent No. 5,549,905
https://patentimages.storage.googleapis.com/d4/c9/82/05d9c5fa9238b2/US5549905.pdf

US005549905A

United States Patent [19]

Mark et al.

[11] Patent Number: 5,549,905

[45] Date of Patent: Aug. 27, 1996

[54] **ENTERNAL COMPOSITION FOR PEDIATRIC PATIENTS**

[75] Inventors: **David A. Mark**, Oak Park; **Diana Twyman**, Chicago; **Donna Buckley**, Barrington, all of Ill.

[73] Assignee: **Clintec Nutrition Co.**, Deerfield, Ill.

[21] Appl. No.: **324,727**

[22] Filed: **Oct. 18, 1994**

[51] **Int. Cl.**[6] **A61K 47/00**

[52] **U.S. Cl.** **424/439**; 514/23

[58] **Field of Search** 424/439; 514/23

[56] **References Cited**

PUBLICATIONS

Ross Products Division, Abbott Laboratories, *Pediasure®Complete Liquid Nutrition*Brochure (1993).

Ross Laboratories, Division of Abbott Laboratories, *Pediasure®, Liquid Nutrition for Children*Brochure (1989).

Primary Examiner—Paul J. Killos

[57] **ABSTRACT**

The present invention provides a method and nutritional composition for providing nutrition to pediatric patients. The methods of the present invention are directed to pediatric patients with impaired nutrient absorption and/or reduced gastrointestinal tolerance. Pursuant to the present invention, the enteral composition includes a hydrolyzed protein source comprising approximately 12% of the total calories, a carbohydrate source and a lipid source comprising a mixture of medium and long chain triglycerides, wherein at least 55% of the lipid source are medium chain triglycerides.

20 Claims, No Drawings

ENTERNAL COMPOSITION FOR PEDIATRIC PATIENTS

BACKGROUND OF THE INVENTION

The present invention relates generally to the treatment and nutritional support of patients. More specifically, the present invention relates to providing nutrition to pediatric patients.

The measurement of diet adequacy in patients, especially pediatric patients, is difficult. Increases in a child's weight and length only grossly reflect nutritional progress. The daily requirements for adequate nutrition are especially significant for the growing child compared with the adult. The relative need for protein, vitamins and minerals remains constant and is greater than that of adults. Moreover, requirements for various vitamins depend on the intake of calories, protein, fat, carbohydrate and specific amino acids.

While the nutritional- needs of the pediatric patient differ from adult patients, in health care settings, adult nutritional formulas are the primary form of elemental nutrition currently being used for children. Naturally, adult formulas do no take into effect the known nutritional needs of the pediatric patient. These adult enteral nutritional products must be diluted to decrease concentrations of, for example, protein, sodium, chloride and the renal solute load levels recommended for children. This dilution reduces the concentrations of other needed nutrients that are often already in concentrations too low for children (i.e. calcium and phosphorous). Thus, providing a nutritional formula designed specifically for children would be advantageous.

A whole protein enteral formula sold under the trademark PEDIASURE® is currently available from Ross Laboratories for nutritional therapy of pediatric patients. pEDIASURE® contains 12% protein, 44% carbohydrates, and 44% fat. The whole protein formula has a protein composition of 82% casein and 18% whey.

Although PEDIASURE® is formulated for children, it is designed to provide nutrition for a limited population, namely 1 to 6 years old. As a result thereof, while PEDIASURE® may meet the National Academy of Sciences-National Research Council (NAS-NRC) Recommended Daily Allowances (RDAs) for children 1 to 6 years old in 1000 calories, it requires 1300 calories to meet the RDA of children ages 7 to 10 years.

Moreover, due to the whole protein nature of PEDIASURE® eand other currently used nutritional products, such products do not meet the nutritional needs of certain pediatric patients. Many pediatric patients have health conditions that impair nutrient absorption and/or reduce gastrointestinal tolerance for diets which are based on whole proteins as well as long-chain fatty acids and/or complex carbohydrates. Examples of the diseases and conditions include, but are not limited to, Crohn's disease, cystic fibrosis, short bowel syndrome, cerebral palsy, HIV/AIDS, chronic diarrhea and gastric reflux.

Therefore, a need exists for a nutritional formula designed to meet the nutritional needs of a larger base of pediatric patients as well as pediatric patients with impaired nutrient absorption and/or reduced gastrointestinal tolerance.

SUMMARY OF THE INVENTION

The present invention provides a nutritional composition designed for pediatric patients. Additionally, the present invention provides a method for providing nutrition to a pediatric patient. The present invention also provides a method for providing nutrition to a pediatric patient with impaired nutrient absorption or reduced gastrointestinal tolerance.

In an embodiment, the present invention provides an enteral composition designed for pediatric patients. The enteral composition includes: a hydrolyzed protein source comprising approximately 12% of the total calories; a carbohydrate source; and a lipid source comprising a mixture of medium and long chain triglycerides, wherein at least 55% of the lipid source are medium chain triglycerides.

In an embodiment, the hydrolyzed protein source is hydrolyzed whey.

In an embodiment, the carbohydrate source is either maltodextrin or corn starch. The carbohydrate source comprises approximately 40% to 60% of the total calories of the composition.

In an embodiment, the lipid source comprises approximately 30% to 40% of the total calories of the composition.

In an embodiment, long chain triglycerides of the lipid source are selected from the group consisting of soy, canola, residual milk fat, and soy lecithin.

In an embodiment, the composition further comprises an omega-3 to omega-6 fatty acid ratio of approximately 4:1 to 6:1.

Still further, in an embodiment, the composition includes at least 100% of the NAS-NRC RDA for children of all vitamins and minerals.

The present invention also provides a method for providing nutrition to a pediatric patient. The method comprises the step of administering to the patient a therapeutically effective amount of a composition comprising: a hydrolyzed protein source comprising approximately 10% to 14% of the total calories; a carbohydrate source; and a lipid source comprising a mixture of medium and long chain triglycerides. The lipid source includes an omega-3 to omega-6 fatty acid ratio of approximately 4:1 to 6:1 and medium chain triglycerides comprise at least 50% of the lipid source.

Still further, the present invention provides a method for providing nutrition to a pediatric patient with impaired nutrient tolerance or reduced gastrointestinal tolerance. The method comprises the step of administering to the patient a therapeutically effective amount of an enteral composition comprising: a hydrolyzed protein source; a carbohydrate source; and a lipid source. The hydrolyzed protein source comprises approximately 10% to 14% of the total calories of the composition. The lipid source comprises a mixture of medium and long chain triglycerides. The medium chain triglycerides make up at least 55% of the lipid source. In a preferred embodiment, the MCT content is at least 60% of the lipid source.

An advantage of the present invention is that it provides a nutritional composition that is ready-to-use, nutritionally complete, and contains proteins, lipids, carbohydrates and vitamins and minerals in proportions appropriate for children ages 1–10 years.

Moreover, an advantage of the present invention is that it provides a nutritional diet for tube and oral use designed for optimal tolerance and absorption in children ages 1–10 years.

Another advantage of the present invention is that it provides a composition including a protein source in a percentage that is adequate to support growth and moderate needs for tissue repair without imposing an undue nitrogen burden on renal function.

Furthermore, an advantage of the present invention is that it provides a composition utilizing hydrolyzed whey protein, medium chain triglycerides and maltodextrin to enhance absorption and reduce intolerance.

Yet another advantage of the present invention is that it includes beta-carotene, thereby allowing for the maintenance of plasma beta-carotene concentration in the pediatric patient.

Still another advantage of the present invention is that it possesses an increased amount of sodium than past formulas, resulting in maintainence of plasma sodium concentration within normal range.

Additional features and advantages of the present invention are described in, and will be apparent from, the detailed description of the presently preferred embodiments.

DETAILED DESCRIPTION OF THE PRESENTLY PREFERRED EMBODIMENTS

Nutritional support of hospitalized children requires prevention, recognition, and treatment of the nutritional depletion that may occur with illness. The goals of nutritional support include stabilizing metabolic state, maintaining body mass, and/or facilitating growth in the presence of disease and gastrointestinal dysfunction.

While nutritional deficiency diseases are unusual in our culture today, other disease states exist that alter intake, absorption or metabolism. As set forth above, certain health conditions can impair the nutrient absorption and/or reduce gastrointestinal tolerance for diets which are based on whole proteins, long-chain fatty acids and/or complex carbohydrates.

The inventors believe that the enteral diet of the present invention when administered to pediatric patients suffering from impaired nutrient absorption and/or reduced gastrointestinal tolerance will provide adequate nutritional support to such patients. Specifically, the inventors believe that the use of the composition of the present invention containing specific protein, carbohydrate and fat sources as well as a source of vitamins and minerals provides an effective nutritional support for pediatric patients.

The protein source of the present invention provides approximately 10% to 14% of the total calories of the composition. In an embodiment, the protein source comprises approximately 12% of the total calories of the composition. This protein concentration chosen is adequate to support growth and moderate needs for tissue repair without imposing an undue nitrogen burden on renal function for children ages 1–10 years.

The protein source is a hydrolyzed protein. In an embodiment, the hydrolyzed protein source is hydrolyzed whey. This type of protein source reduces the incidence of gastric reflux because gastric emptying is faster than with diets containing casein or whole whey. Also, hydrolyzed whey protein serves as a rich source of amino acid cysteine. Cysteine is a limiting amino acid for the formation of glutathione, and glutathione needs may be higher in children with infectious or inflammatory conditions. In an embodiment, the composition of the present invention contains approximately 0.27% of calories as cysteine (approximately 690 mg per 1000 calories).

Carbohydrates provide approximately 40% to 60% of the caloric content of the composition. In an embodiment, the carbohydrate source is approximately 55% of the caloric content of the composition. A number of carbohydrates can be used including maltodextrin or hydrolyzed corn starch.

The lipid source includes a mixture of medium chain triglycerides (MCT) and long chain triglycerides (LCT). The lipid source of the present invention is approximately 30% to about 40% of the caloric content of the composition. In an embodiment, the lipid source of is approximately 33% of the caloric content of the composition. The lipid profile is designed to meet essential fatty acid needs (omega-3 and omega-6) while also keeping MCT content high and LCT content low compared with prior formulas.

The lipid source includes at least 50% from medium chain triglycerides. In an embodiment, MCTs make up at least 55% of the lipid source. In a preferred embodiment, the lipid source includes at least 60% from MCTs. The lipid profile is designed to set the MCT content at approximately 60% of lipid content by weight. This limits MCT to under 20% of total calories, thereby reducing the risk of gastrointestinal intolerance. In a preferred embodiment, the medium chain triglyceride source is fractionated coconut oil.

Suitable sources of long chain triglycerides are canola oil, soy oil, residual milk fat, and soy lecithin.

The lipid profile containing such long chain triglycerides is designed to have a polyunsaturated fatty acid omega-6 (n-6) to omega-3 (n-3) ratio of approximately 4:1 to 6:1. In an embodiment, the n-6 to n-3 fatty acid ratio is approximately 5:1. Both the omega-6 and omega-3 fatty acids are provided in sufficient quantity to meet tissue growth maintenance needs. To this end, in an embodiment, the source of omega-6 fatty acids is present in a range of approximately 4–6% of the total calories. The omega-3 fatty acid source is preferably present in the range of approximately 0.8–1.2% of the total calories. In addition to the absorption/tolerance benefits of a relatively low LCT content, the composition of the present invention is less likely to be immunosuppressive due to the low percentage of omega-6 fatty acids.

By way of example, and not limitation, an example of a fatty acid lipid profile that may be used in the composition of the present invention will now be given.

	LIPID PROFILE (38.5 g/L)		
LIPID	% of Total Fatty Acids	g/1000 ml	% OF KCAL
C6:0	0.8	0.3	
C8:0	29.1	11.2	
C10:0	20.6	7.9	
C12:0	1.2	0.5	
C14:0	0.6	0.2	
C16:0	3.8	1.5	
C18:0	1.7	0.7	
TOTAL SAT	57.8	22.3	21.6%
C16:1	0.1	0.0	
C18:1	13.4	5.2	
TOTAL MONO	13.5	5.2	5.6%
C18:2 n6	12.2	4.7	4.9%
C18:3 n3	2.4	0.9	0.9%
TOTAL POLY	14.6	5.6	5.8%
TOTAL	86.0	33.1	33.0%

Still further, the present invention, in an embodiment, includes a specialized vitamin and mineral profile. The composition includes a source of vitamins and minerals providing at least 100% of the NAS-NRC Recommended Daily Allowance for children. The vitamin and mineral requirements are met in 1000 kcal per day because this

intake is practical, achievable and easily tolerated by children ages 1–10 years, even though it is somewhat less than healthy children normally eat. Unlike prior compositions, the composition of the present invention meets NAS-NRC RDAs for children ages 1–10 years in 1000 calories. The high vitamin and mineral concentration of the present invention is of practical benefit because typical feeding regimens (e.g. 50mL/hour for 20 hours/day) will meet all needs. However, none of the vitamin or mineral concentrations are so high that there is any risk of approaching toxic levels, even at 2000–2500 kcal per day.

In an embodiment, the composition of the present invention includes a source of beta-carotene. The inventors view beta-carotene, formerly considered only as a precursor to vitamin A, as an important nutrient with anti-oxidant properties. In an embodiment, the composition includes approximately 0.5–2.0 mg of betacarotene per 1000 calories. This amount of beta-carotene is sufficient to maintain plasma beta-carotene concentration in the pediatric patient.

The composition of the present invention, in an embodiment, includes certain electrolyte concentrations. The electrolyte concentrations are set to meet needs without providing an undue renal solute burden on kidney function. To this end, sodium is preferably present in a range of approximately 420–500 mg/L. In an embodiment, potassium and chloride are present at ranges of approximately 2060–380 mg/L and 1040–1120 mg/L, respectively. The renal solute load is, in an embodiment, present in a range of approximately 200–210 mOsm. In a preferred embodiment, the electrolyte concentrations of the present invention are as follows: sodium is present at 460 mg/L; potassium is present at 320 mg/L; chloride is present at 1080 mg/L; and the renal solute load is at 205 mOsm.

The composition of the present invention is a ready-to-use enteral formulation. The composition can be used as a supplement or for total enteral nutritional support. The composition can be tube-fed to a patient, or fed by having the patient drink same. Preferably, the caloric density of the composition is 1.0 kcal/ml.

The composition of the present invention can be used for providing nutrition to a pediatric patient ages 1 to 10 years. Likewise, the composition can be used for providing nutrition to a pediatric patient with impaired nutrient absorption and/or reduced gastrointestinal tolerance. The diet utilizes hydrolyzed whey protein, medium chain triglycerides and maltodextrin to enhance absorption and reduce intolerance.

By way of example, and not limitation, an example of a suitable composition that may be used pursuant to the present invention is as follows:

The composition includes the following ingredients: protein: whey; carbohydrate: maltodextrin, sucrose, corn starch; lipid: safflower oil, canola oil, soy oil, coconut oil (MCT), residual milk fat, soy lecithin; water; vitamin A (retinol); beta-carotene; vitamin D, vitamin E; vitamin K; vitamin C; thiamine B_1; riboflavin B_2; niacin; vitamin B_6; folic acid; pantoth acid; vitamin B_{12}; biotin; choline; taurine; L-carnitine; inositol; calcium; phosphorus; magnesium; zinc; iron; copper; manganese; iodine; sodium; potassium; chloride; chromium; molybdenum; and selenium.

The composition of the present invention has the following nutrient composition (per 1000 calories):

NUTRIENT COMPOSITION	AMOUNT#
CAL. DENSITY	1.0 (kcal/ml)
PROTEIN	30.0(12%) g(%)
WHEY	100%
CARBOHYDRATE	137.5(55%) g(%)
LIPID	38.5(33%) g(%)
SAFFLOWER OIL	—
CANOLA OIL	13%
SOY OIL	16%
COCONUT OIL MCT	60%
RESIDUAL MILK FAT	6%
SOY LECITHIN	5%
N6:N3 RATIO	5:1
WATER	850 ml
VITAMIN A (RETINOL)	2400 IU
BETA-CAROTENE	1.0 mg
VITAMIN D	560 IU
VITAMIN E	28 IU
VITAMIN K	30 mcg
VITAMIN C	100 mg
THIAMINE B_1	2.4 mg
RIBOFLAVIN B_2	2.0 mg
NIACIN	20 mg
VITAMIN B_6	2.4 mg
FOLIC ACID	400 mcg
PANTOTH. ACID	10 mg
VITAMIN B_{12}	6 mcg
BIOTIN	300 mcg
CHOLINE	300 mg
TAURINE	80 mg
L-CARNITINE	40 mg
INOSITOL	80 mg
CALCIUM	1000 mg
PHOSPHORUS	800 mg
Ca:P	1.25:1 weight
MAGNESIUM	200 mg
ZINC	15 mg
IRON	14 mg
COPPER	1.0 mg
MANGANESE	1.5 mg
IODINE	120 mcg
SODIUM	460 mg
POTASSIUM	1320 mg
CHLORIDE	1080 mg
Na:K	0.59:1 molar
(Na + K)/Cl	1.71 molar
CHROMIUM	30 mcg
MOLYBDENUM	30 mcg
SELENIUM	30 mcg

It will be understood that various modifications to the presently preferred embodiments described herein will be apparent to those skilled in the art. Such changes and modifications can be made without departing from the spirit and scope of the present invention and without diminishing its attendant advantages. It is therefore intended that such changes and modifications be covered by the appended claims.

We claim:

1. An enteral composition designed for pediatric patients comprising:

a hydrolyzed protein source comprising approximately 12% of the total calories;

a carbohydrate source; and

a lipid source comprising a mixture of medium and long chain triglycerides, wherein at least 55% of the lipid source are medium chain triglycerides.

2. The composition of claim **1** wherein the hydrolyzed protein source is hydrolyzed whey.

3. The composition of claim **1** further comprising a source of beta-carotene.

4. The composition of claim 1 wherein the carbohydrate source is selected from the group consisting of: maltodextrin and corn starch.

5. The composition of claim 1 wherein the long chain triglycerides are selected from the group consisting of soy, canola, residual milk fat, and soy lecithin.

6. The composition of claim 1 further comprising an omega-6 to omega-3 fatty acid ratio of approximately 4:1 to 6:1.

7. The composition of claim 1 further comprising at least 100% of the NAS-NRC RDA of all vitamins and minerals in approximately 1000 calories.

8. The composition of claim 1 further comprising omega-6 fatty acids present in an amount of approximately 4 to 6% of the total calories.

9. A method for providing nutrition to a pediatric patient comprising the step of administering to the patient a therapeutically effective amount of a composition comprising:

a hydrolyzed protein source comprising approximately 10% to 14% of the total calories;

a carbohydrate source; and

a lipid source comprising a mixture of medium and long chain triglycerides, wherein at least 50% of the lipid source are medium chain triglycerides and the lipid source includes an omega-6 to omega-3 fatty acid ratio of approximately 4:1 to 6:1.

10. The method of claim 9 wherein the hydrolyzed protein source is hydrolyzed whey.

11. The method of claim 9 wherein the lipid source comprises approximately 33% of the total calories.

12. The method of claim 9 further comprising a source of beta-carotene.

13. The method of claim 9 further comprising at least 100% of the NAS-NRC RDA of all vitamins and minerals in approximately 1000 calories.

14. The method of claim 9 further comprising omega-6 fatty acids present in an amount of approximately 4 to 6% of the total calories.

15. A method for providing nutrition to a pediatric patient with impaired nutrient absorption or reduced gastrointestinal tolerance comprising the step of administering to the patient a therapeutically effective amount of a composition comprising:

a hydrolyzed protein source comprising approximately 12% of the total calories;

a carbohydrate source; and

a lipid source comprising a mixture of medium and long chain triglycerides, wherein at least 55% of the lipid source are medium chain triglycerides.

16. The method of claim 15 wherein the hydrolyzed protein source is hydrolyzed whey.

17. The method of claim 15 further comprising an omega-6 to omega-3 fatty acid ratio of approximately 4:1 to 6:1.

18. The method of claim 15 further comprising a source of beta-carotene.

19. The method of claim 15 further comprising at least 100% of the NAS-NRC RDA of all vitamins and minerals in approximately 1000 calories.

20. The method of claim 15 further comprising omega-6 fatty acids present in an amount of approximately 4 to 6% of the total calories.

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ANNEX G:

Decision of the Patent Trial and Appeal Board at USPTO, dispatched on April 15, 2016

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte URVASHI BHAGAT

Appeal 2016-004154
Application 12/426,034
Technology Center 1600

Before RICHARD M. LEBOVITZ, JEFFREY N. FREDMAN, and JOHN G. NEW, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal[1] under 35 U.S.C. § 134 involving claims to lipid-containing formulations. The Examiner rejected the claims as directed to a product of nature and as anticipated. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

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[1] Appellant identifies the Real Party in Interest as Asha Nutrition Sciences, Inc. (*see* App. Br. 3).

Statement of the Case

Background

"Linoleic acid (LA) and Alpha-linolenic Acid (ALA) are the precursors for all omega-6 and omega-3 fatty acids. It is well established that LA and ALA are 'essential' fatty acids" (Spec. ¶ 4). "Dietary deficiency or excess of the two essential fatty acids may cause many illnesses" (Spec. ¶ 4).

The Claims

Claims 52, 61, 64, 65, 67–69, 73–75, 77, 78, 80, 82, 83, 90–102, 107, 116–122, 124, and 128–145 are on appeal. Independent claim 65 is representative and reads as follows:

> 65. A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4: 1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids from different sources, and wherein
>
> > (1) omega-6 fatty acids are 4–75% by weight of total lipids and omega-3 fatty acids are 0.1–30% by weight of total lipids; or
> >
> > (2) omega-6 fatty acids are not more than 40 grams.

The Issues

A. The Examiner rejected claims 52, 61, 64, 65, 67–69, 73–75, 77, 78, 80, 82, 83, 90–102, 107, 116–122, 124, and 128–145 under 35 U.S.C. § 101 as directed to non-statutory subject matter (Ans. 6–22).

B. The Examiner rejected claims 52, 61, 64, 65, 67–69, 73, 75, 77, 78, 80, 83, 90, 92–96, 98, 100, 129–131, 133–137, 142, and 144 under

35 U.S.C. § 102(b) as anticipated by Mark[2] (Ans. 47–53).

C. The Examiner rejected claims 52, 61, 64, 65, 67–69, 73–75, 77, 78, 80, 82, 83, 90, 92–94, 96–98, 100, 129–131, 133, 136, 137, 142, and 144 under 35 U.S.C. § 102(b) as anticipated by Olives[3] as evidenced by "Olives Nutrient Analysis"[4] (Ans. 65–72).

D. The Examiner rejected claims 52, 61, 64, 65, 67–69, 73–75, 77, 78, 80, 83, 90–101, 116–118, 120–122, 124, 128–140, and 141–145 under 35 U.S.C. § 102(b) as anticipated by Walnuts[5] as evidenced by "Walnut Nutrient Analysis"[6] (Ans. 73–83).

A. 35 U.S.C. § 101

The Examiner finds that

> a one ounce serving of walnut oil (28 grams, i.e. a 'dosage') is a lipid-containing formulation that contains 28 gm of fatty acids (lipids) and ~ 50 mg of "other" lipids . . . . The ratio of omega-6 to omega-3 fatty acids is 5.09:1 (i.e. 4:1 or greater). Walnut oil contains 14.81 grams (52.8% by weight; i.e.

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[2] Mark et al., US 5,549,905, issued Aug. 27, 1996 ("Mark").
[3] Olives, web.archive.org/web/20060314112112/http://www.whfoods.com/genpage.php?pfriendly=1&tname=foodspice&dbid=46 (Mar. 14, 2006). We refer to pages by number in sequential order.
[4] Olives Nutrient Analysis, web.archive.org/web/20060314112106/http://www.whfoods.com/genpage.php?tname=nutrientprofile&dbid=111 (Mar. 14, 2006).
[5] Walnuts, http://www.whfoods.com/genpage.php?tname=foodspice&dbid=99 (Nov. 9, 2006).
[6] Walnut Nutrient Analysis, http://web.archive.org/web/20061109221127/http://www.whfoods.com/genpage.php?tname=nutrientprofile&dbid=132 (Nov. 9, 2006).

> between 4 and 75% by weight of total lipids, or, greater than 20% by weight of total lipids) of omega-6 fatty acids. Walnut oil contains 2.91 grams (10% by weight of total lipids) of omega-3 fatty acids.

(Ans. 12). The Examiner finds that "walnut oil is a judicial exception (i.e. a product of nature)" (Ans. 18) and that "the claimed composition does not have markedly different characteristics from what occurs in nature" (Ans. 16).

Appellant contends that

> The claims include several elements that add significantly more than what occurs in nature, such as "intermixtures of lipids from different sources", "a dosage of omega-6 /omega-3 fatty acids", "a ratio of omega-6 to omega-3 fatty acids of 4: 1 or greater" or "omega-6 fatty acids greater than 20% by weight of total lipids", "contained in one or more complementing casings providing controlled delivery of the formulation to a subject," with defined "dosages" and defined concentrations.

(App. Br. 8).

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that the claims are drawn to products of nature, a class of non-statutory subject matter?

Findings of Fact

1. The Specification teaches that "the lipid formulation disclosed herein may be administered to an individual in any orally accepted form" (Spec. ¶ 34).

2. The Specification teaches that the "fatty acid components of the composition's lipid contents are achieved at least in part by using one or

more of the following concentrated lipid sources: oils, butters, nuts, and seeds" (Spec. ¶ 9).

3. The Specification teaches that "synergy among complementing nutrients from different sources may be incorporated. Furthermore, using different sources avoids concentrated delivery of specific phytochemicals that may be harmful in excess" (Spec. ¶ 30).

4. The Erickson Declaration 3/31/15[7] states "'[d]ifferent sources' refers to different oils, butters, nuts, seeds, herbs, sweeteners, and/or other foods and/or their different varieties (containing different lipid profiles)" (Erickson Decl. 3/31/15 ¶ 6; *cf.* Rucker Decl. 4/30/15[8] ¶ 6); and Das Decl. 4/30/15[9] ¶ 6).

5. The Erickson Declaration 3/31/15 states that "each walnut (or olive) would not be considered to be a different source of lipids from one another by skilled artisans, unless one specific variety of walnut (or olive) is added to another, different, specific variety of walnuts (or olives) to enhance usefulness of the walnut (or olive) formulation" (Erickson Decl. 3/31/15 ¶ 7; *cf.* Rucker Decl. 4/30/15 ¶ 9; and Das Decl. 4/30/15 ¶ 9).

6. The Erickson Declaration 1/31/14[10] states that "[l]ipid content, including omega-6 and omega-3, of products of nature is extremely variable. This variability depends on the source, background genetics, cultivating conditions, including soils, fertilizer used, and other variable factors, such as hours of sunlight and water composition" (Erickson Decl. 1/31/14 ¶ 3).

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[7] Declaration of Dr. Kent L. Erickson, dated May 31, 2015.
[8] Declaration of Dr. Robert B. Rucker, dated Apr. 30, 2015.
[9] Declaration of Dr. Undurti N. Das, dated Apr. 30, 2015.
[10] Declaration of Dr. Kent L. Erickson, dated Jan. 31, 2014.

7. Walnut Oil Nutrition Facts[11] teaches that walnut oil contains 14810 mg omega-6 fatty acids and 2912 mg omega-3 fatty acids resulting in a ratio of approximately 5:1 omega 6 to omega 3 fatty acids with less than 40 grams of omega-6 fatty acids (Walnut Oil Nutrition Facts 2).

8. Olive Oil Nutrition Facts[12] teaches that olive oil contains 2734 mg omega-6 fatty acids and 213 mg omega-3 fatty acids resulting in a ration of ~ 12.8:1 omega 6 to omega 3 fatty acids with less than 40 grams of omega-6 fatty acids (Olive Oil Nutrition Facts 2).

Principles of Law

In *Funk Bros.*, "bacteria produced by the laboratory methods of culture are placed in a powder or liquid base and packaged for sale to and use by agriculturists in the inoculation of the seeds of leguminous plants." *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 129 (1948). "The qualities of these bacteria, like the heat of the sun, electricity, or the qualities of metals, are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none." *Id.* at 130.

"[E]xtensive effort alone is insufficient to satisfy the demands of § 101. Nor are Myriad's claims saved by the fact that isolating DNA from the human genome severs chemical bonds and thereby creates a nonnaturally occurring molecule." *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2118 (2013). "Myriad's claims are simply not

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[11] Oil, vegetable, walnut, http://nutritiondata.self.com/facts/fats-and-oils/589/2 (accessed Feb. 11, 2015).
[12] Oil, olive, salad or cooking, http://nutritiondata.self.com/facts/fats-and-oils/509/2 (accessed Feb. 11, 2015).

expressed in terms of chemical composition, nor do they rely in any way on the chemical changes that result from the isolation of a particular section of DNA." *Id.*

Analysis

i. Claim Interpretation

We begin with claim interpretation of the disputed claim phrase "intermixture of lipids from different sources" in claim 65 regarding the meaning of "different sources" and whether "intermixture of lipids" represents a product-by-process limitation.

"intermixture of lipids"

Claim 65 is drawn to a "lipid-containing formulation," not a process for making the composition. The weight of authority holds that the patentability of product-by-process claims is not dependent on process limitations. *See In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985) ("even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself"; "[t]he patentability of a product does not depend on its method of production"; and "[i]f the product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.")

We agree with the Examiner that "any prior art lipid-containing formulation from a single source that occurs in nature but appears to be structurally the same, i.e. contains the same lipid components . . . is considered to read on these claims" (Ans. 4; emphasis omitted). Appellant does not identify any necessary structural differences in the final "lipid-

containing formulation" that results based upon the use of an "intermixture of lipids from different sources." For example, Appellant does not explain or provide evidence that a container of olive oil pressed from a single tree of Kalamata olives necessarily differs in lipid content from a container of blended olive oil pressed from an intermixture of different varieties of olives such as Kalamata, Nicoise, Picholine, and Manzanilla olives (*see* Olives 3).

We recognize, but find unpersuasive, Appellant's reliance upon the Erickson Declaration 3/31/15 teaching that "when lipids from different sources are intermixed, the resulting mixture will necessarily have different physical and chemical properties from a 'single' source" (Erickson Decl. 3/31/15 ¶ 8; *cf.* App. Br. 16–17). It is the composition which is being claimed. Appellant has not provided adequate evidence that an oil from different sources would necessarily have a composition that is different from one from the same source, nor that a different source would necessarily impart characteristics to the formulation which were absent when a single source was used.

If the term "different sources" is read so narrowly as to require any differences, distinguish single component or "intermixture" sources, then the Examiner's broad interpretation discussed above demonstrates natural products with "different sources." Alternatively, if the "intermixture" refers to the final product, which may be obtained in different ways by adding different amounts of components to obtain the desired composition, then the Examiner's product-by-process reasoning applies.

"casing" and "dosage"

The Specification does not provide a definition of the term "casing," expressly stating that any "orally accepted form" falls within the scope of the invention (FF 1). Additionally, claim 65 does not require any particular dosage of the formulation, so long as there are not more than 40 grams of omega-6 fatty acids.

Considering claim 65 as a whole, we agree with the Examiner that whether the lipid-containing formulation with a "dosage" of omega-6 and omega-3 fatty acids in a "casing" and derived from an "intermixture of lipids from different sources" is interpreted as a product-by-process claim (*see* Ans. 4).

ii. Product of Nature

We are constrained by the Supreme Court decisions in *Funk Bros.* and *Myriad* to agree with the Examiner that walnut oil is a "product of nature" falling within the judicial exception to patentable subject matter.

In *Funk Bros.*, "products of nature" included bacteria that were "produced by the laboratory methods of culture" and "placed in a powder or liquid base and packaged for sale to and use by agriculturists in the inoculation of the seeds of leguminous plants." *Funk Bros. Seed Co.*, 333 U.S. at 129. Thus, the Supreme Court did not find routine production and extraction steps resulted in a product that was "markedly different" from the product of nature.

In *Myriad*, "products of nature" included isolated DNA that was extracted from cells and required "sever[ing] chemical bonds and thereby creat[ing] a nonnaturally occurring molecule." *Myriad*, 133 S. Ct. at 2118.

Again, the Supreme Court did not find that routine production and extract steps resulted in a product, finding that the "processes used by Myriad to isolate DNA were well understood by geneticists at the time of Myriad's patents." *Id.* at 2119.

Appellant contends that walnut "oil extraction is a complex multi-step process during which physical and chemical properties of the plant seeds, such as walnuts and olives, transform dramatically producing oils and by-products" (App. Br. 9). Appellant contends that "[t]hus, extracted oils, including Walnut Oil and Olive Oil are man-made products not products of nature and they have markedly different characteristics than products of nature, such as some walnuts/olives" (App. Br. 11).

We are not persuaded. The Examiner notes that "there are no limitations in the claims requiring any alleged sources of lipids to be prepared by the oil extraction processes described" (Ans. 23) and the ordinary artisan would recognize that some oils, like extra virgin olive oil, are "the initial unrefined oil from the first pressing" (Olives 3).

We recognize, but find unpersuasive, Appellant's contention that "isolated individual omega-6, omega-3, other fatty acids, or other lipids, or naturally occurring plant/animal parts <u>are</u> judicial exceptions, but composites of such matters <u>are not</u> judicial exceptions" (App. Br. 12). Consistent with Supreme Court precedent, some processing such as the walnut oil refining, may not result in a "markedly different" product as evidenced by the laboratory culture, powder, and packaging of bacteria in *Funk Bros.* or the chemical isolation and cleavage of DNA in *Myriad*. We see no principled reasoning that supports finding walnut or olive oil "markedly different"

while finding the packaged and powdered bacteria of *Funk Bros.* or the isolated DNA of *Myriad* not "markedly different."

We recognize, but find unpersuasive, Appellant's contention that "even within the same species lipid content, including omega-6 and omega-3, of natural plant seeds and their oils cannot be predicted" (App. Br. 20). In this case, the Examiner relies upon evidence of particular compositions of walnut oil or olive oil that satisfy the requirements of claim 65 (FF 7–8). That other natural compositions may not fall within the scope of the claim is irrelevant because the exception is to any product of nature, not all products of nature.

We recognize, but find unpersuasive, Appellant's contention that the "products of instant claims serve the function of solving a long-felt critical unmet need" (App. Br. 21; *cf.* App. Br. 32–33). Long-felt need and secondary considerations are doctrines related to obviousness that do not apply to either utility or anticipation. *See Cohesive Techs., Inc. v. Waters Corp.* 543 F.3d 1351, 1364 (Fed. Cir. 2008) ("[O]bviousness requires analysis of secondary considerations of nonobviousness, while secondary considerations are not an element of a claim of anticipation.")

We recognize, but find unpersuasive, Appellant's contention that the "Examiner has rebuffed overwhelming evidence and testimony of skilled persons regarding the presence of not well-understood, non-routine, and non-conventional features in the claimed formulations, which confers patent eligibility based on case law" (App. Br. 22; emphasis omitted). Rather, the Examiner, constrained by *Funk Bros.* and *Myriad*, carefully considered the Declarations of Dr. Erickson, Rucker, and Das (*see* Ans. 26, 30, 31, 38) but

found the evidence supported the § 101 "product of nature" rejection. We have also carefully reviewed these expert Declarations, and find them unpersuasive for the reasons given above.

We recognize, but find unpersuasive, Appellant's contention that the prior art "specifically teaches against high omega-6 to omega-3 ratios, and places emphasis on low ratios of the fatty acids not amounts/dosages" (App. Br. 23; emphasis omitted). Just as "[t]eaching away is irrelevant to anticipation." *Seachange Int'l, Inc., v. C-COR, Inc.*, 413 F.3d 1361, 1380 (Fed. Cir. 2005), teaching away is also irrelevant to the issue of patentable subject matter. Either the claims read on products of nature or they do not.

We recognize, but find unpersuasive, Appellant's contention that "the prior art neither understood the importance of omega-6, nor its relationship with other lipids; and the prior art routinely recommended use of other lipids that suppress omega-6 activity" (App. Br. 28). This argument is irrelevant to the issue of statutory subject matter and utility, because significant or not, the issue is whether the claimed formulation reads on a "product of nature" not whether that formulation has unexpected properties.

Appellant separately argue the limitations of dependent claims 67 and 68 (App. Br. 35), but do not rebut the Examiner's finding that "there is no evidence in the specification that combining walnut oil with any source of naturally occurring proteins and carbohydrates, in any amounts, results in a marked change in function" (Ans. 19). The Examiner's reasoning is consistent with *Funk Bros.*, where the combination of natural occurring bacteria did not overcome the lack of statutory subject matter. *See Funk Bros.*, 333 U.S. at 131 ("The bacteria perform in their natural way. Their use

in combination does not improve in any way their natural functioning. They serve the ends nature originally provided and act quite independently of any effort of the patentee.")

Appellant argues that claim 77 differs as "one-part or [comprises] multi-part" components (App. Br. 35). We are not persuaded because the walnut or olive oils teach one ounce serving sizes that are reasonably interpreted as one-part dosages (*see* Walnut Oil 1).

Appellant contends that claims 78 and 124 "cannot be said to provide steady delivery of the claimed formulation" (App. Br. 35). Appellant provides no evidence that the natural compositions fail to satisfy this claim limitation. *See In re De Blauwe*, 736 F.2d 699, 705 (Fed. Cir. 1984) (Arguments and conclusions unsupported by factual evidence carry no evidentiary weight.)

Appellant points to limitations in claims 102, 107, and 119, but does not identify any evidence that these limitations distinguish from the disclosed walnut or olive oils.

Appellant contends, regarding claim 128, that "at least some varieties of almonds, peanuts, and coconuts, and their oils, have no omega-3 content at all, and that their omega-6 concentration is at most 32%" (App. Br. 36). We find this argument unpersuasive because the claim 128 is drawn to a formulation that may include olive oil and walnut oil expressly, and Appellant has provided no evidence of necessary structural difference based on the product-by-process language. *In re Thorpe*, 777 F.2d at 697.

Appellant contends regarding claims 136 and 139 that regarding starches and sugars, "[t]here is no evidence that any product of nature meets

this requirement" (App. Br. 36). We agree with the Examiner that "[t]here is no evidence of record that including, for example, ANY naturally occurring sugar or starch, in ANY amount, with the lipid-containing formulations of Claims 65 and 91 would result in a marked change in the characteristics of walnut oil (or olive oil)" (Ans. 45). The Examiner's reasoning remains consistent with *Funk Bros.*, where the combination of natural occurring bacteria did not overcome the lack of statutory subject matter. *See Funk Bros.*, 333 U.S. at 131.

We remain unpersuaded by Appellant's reiteration of their argument on the scope of "intermixed" for claims 142 and 144 for the reasons already given above (*see* App. Br. 36).

Conclusion of Law

The evidence of record supports the Examiner's conclusion that the claims are drawn to products of nature, a class of non-statutory subject matter.

B. 35 U.S.C. § 102(b) over Mark

The Examiner finds that:

> Mark teaches the detailed lipid profile of the 38.5 g lipid component in the one liter (1000 ml) oral pediatric composition (column 4, lines 40 - 60) as containing 12.2% omega-6 fatty acids and 2.4% omega-3 fatty acids based on total lipids, thus meeting limitation (1) recited in instant Claims 65 and limitation (i) and (ii) of instant Claim 83. Further, it is noted that the amount by weight of omega-6 fatty acids is 4.70g (12.2% of 38.5 g) and the amount by weight omega-3 fatty acids is 0.924 g (38.5 g x 2.4%) which meets limitation (2) recited in instant Claim 65.

(Ans. 48).

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that Mark anticipates the claims?

Findings of Fact

9. Mark teaches "a nutritional composition designed for pediatric patients" (Mark, col. 1, ll. 65–66).

10. Mark teaches "a lipid source comprising a mixture of medium and long chain triglycerides. The lipid source includes an omega-3 to omega-6 fatty acid ratio of approximately 4:1 to 6:1" (Mark, col. 2, ll. 35–38).

11. Mark teaches that a "lipid profile containing such long chain triglycerides is designed to have a polyunsaturated fatty acid omega-6 (n-6) to omega-3 (n-3) ratio of approximately 4:1 to 6:1" (Mark, col. 4, ll. 21–23).

12. Mark teaches that in "an embodiment, the n-6 to n-3 fatty acid ratio is approximately 5:1. Both the omega-6 and omega-3 fatty acids are provided in sufficient quantity to meet tissue growth maintenance needs" (Mark, col. 4, ll. 23–27).

13. Mark teaches that "the source of omega-6 fatty acids is present in a range of approximately 4–6% of the total calories. The omega-3 fatty acid source is preferably present in the range of approximately 0.8–1.2% of the total calories" (Mark, col. 4, ll. 27–31).

14. Mark teaches "an example of a fatty acid lipid profile that may be used in the composition of the present invention will now be given.

LIPID PROFILE (38.5 g/L)			
LIPID	% of Total Fatty Acids	g/1000 ml	% OF KCAL
C6:0	0.8	0.3	
C8:0	29.1	11.2	
C10:0	20.6	7.9	
C12:0	1.2	0.5	
C14:0	0.6	0.2	
C16:0	3.8	1.5	
C18:0	1.7	0.7	
TOTAL SAT	57.8	22.3	21.6%
C16:1	0.1	0.0	
C18:1	13.4	5.2	
TOTAL MONO	13.5	5.2	5.6%
C18:2 n6	12.2	4.7	4.9%
C18:3 n3	2.4	0.9	0.9%
TOTAL POLY	14.6	5.6	5.8%
TOTAL	86.0	33.1	33.0%

(Mark, col. 4, ll. 35–60).

15. Mark teaches "typical feeding regimens (e.g. 50mL/hour for 20 hours/day)" (Mark, col. 5, ll. 8–9).

16. Mark teaches a composition that "has the following nutrient composition (per 1000 calories)

NUTRIENT COMPOSITION	AMOUNT#
CAL. DENSITY	1.0 (kcal/ml)
PROTEIN	30.0(12%) g(%)
WHEY	100%
CARBOHYDRATE	137.5(55%) g(%)
LIPID	38.5(33%) g(%)
SAFFLOWER OIL	—
CANOLA OIL	13%
SOY OIL	16%
COCONUT OIL MCT	60%
RESIDUAL MILK FAT	6%
SOY LECITHIN	5%
N6:N3 RATIO	5:1
WATER	850 ml
VITAMIN A (RETINOL)	2400 IU
BETA-CAROTENE	1.0 mg
VITAMIN D	560 IU
VITAMIN E	28 IU
VITAMIN K	30 mcg
VITAMIN C	100 mg
THIAMINE B_1	2.4 mg
RIBOFLAVIN B_2	2.0 mg
NIACIN	20 mg
VITAMIN B_6	2.4 mg
FOLIC ACID	400 mcg
PANTOTH. ACID	10 mg
VITAMIN B_{12}	6 mcg
BIOTIN	300 mcg
CHOLINE	300 mg
TAURINE	80 mg
L-CARNITINE	40 mg
INOSITOL	80 mg
CALCIUM	1000 mg
PHOSPHORUS	800 mg
Ca:P	1.25:1 weight
MAGNESIUM	200 mg
ZINC	15 mg
IRON	14 mg
COPPER	1.0 mg
MANGANESE	1.5 mg
IODINE	120 mcg
SODIUM	460 mg
POTASSIUM	1320 mg
CHLORIDE	1080 mg
Na:K	0.59:1 molar
(Na + K)/Cl	1.71 molar
CHROMIUM	30 mcg
MOLYBDENUM	30 mcg
SELENIUM	30 mcg

"

(Mark, col. 6, ll. 1–45).

Principles of Law

"A single prior art reference that discloses, either expressly or inherently, each limitation of a claim invalidates that claim by anticipation." *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1375 (Fed. Cir. 2005).

Analysis

We adopt the Examiner's findings of fact and reasoning regarding the scope and content of Mark (Ans. 47–53; FF 9–16) and agree that the claims are anticipated by Mark. We address Appellant's arguments below.

Dosage

Appellant contends that "[t]here is no 'dosage of omega-6 and omega-3 fatty acids' disclosed anywhere by Mark et al. The table in column 4 of Mark et al. discloses concentration of C18:2 n6, i.e. linoleic acid (not total omega-6), and C18:3 n3, i.e. linolenic acid (not total omega-3) in 86% (not 100%) of the fatty acids (see line 60)" (App. Br. 40).

We are not persuaded. Mark teaches "typical feeding regimens (e.g. 50mL/hour for 20 hours/day)" (FF 15), thereby teaching a typical daily dose of 1,000 ml (50 ml/hour x 20 hours/day). The claims do not require the dosage to be ingested at one time. The table in column 4 of Mark refers to amounts in g/1000 ml, thereby teaching daily amounts typically fed to a child in need of the supplement (FF 14–15). This reasoning is consistent with the Erickson Declaration 3/31/15, which states that "feeding regimen of Mark et al. compositions may be few milliliters for a 1-year old child and few liters for a 10-year old child" (Erickson Decl. 3/31/15 ¶ 15). That is, even the Erickson Declaration 3/31/15 concedes that the ordinary artisan would recognize Mark's dosages may include 1,000 ml (1 liter).

4:1 ratio of Omega-6 to Omega-3

Appellant contends that "the table [in column 4 of Mark] does not expressly state that it discloses the composition of triglycerides, only. It can be concluded that the data in the table in column 4 of Mark et al. is corrupted and not operable due to many errors, such as erroneous use of the term 'TOTAL' in lines 50, 54, and 59, and the missing fatty acids in line 60" (App. Br. 42). Appellant cites the Erickson Declaration 1/31/14 for variability in lipid content (*see* App. Br. 42, Erickson Decl. 1/31/14 ¶ 3). Appellant contends that "[i]t is impossible to guess the composition of the missing 14% of fatty acids in the table in column 4" (App. Br. 43). The Erickson 3/31/15, Rucker 4/30/15, and Das 4/30/15 Declarations each state that "[i]t is not possible to ascertain omega-6 to omega-3 ratio from the table in column 4 because *only* 86% of the fatty acids are disclosed, 14% of the fatty acids are missing" (Erickson Decl. 3/31/15 ¶ 10; *cf.* Rucker Decl. 4/30/15 ¶ 10; Das Decl. ¶ 10).

We are not persuaded for two reasons. First, the Examiner points to the example at column 6, which expressly states that there is a 5:1 ratio of N6:N3, satisfying the ratio requirement of claim 65 (FF 16).

Second, even the table in column 4 of Mark is a specific example of a fatty acid profile with 12.2% omega-6 fatty acids or 4.7 g/1000 ml and 2.4 % omega-3 fatty acids or 0.9 g/1000 ml resulting in a ratio exceeding 4:1 (FF 14). While only 86% of the total fatty acids are shown in table 4 (FF 14), Mark teaches the maximal amounts of total calories for omega-6 and omega-3 fatty acids (FF 13). In particular, Mark teaches a maximal calorie amount of 6% for omega-6 and 1.2% for omega-3 (FF 13). The table in column 4 of

Mark discloses omega-6 fatty acids are 4.9% of total calories and omega-3 fatty acids are 0.9% of total calories.

Thus, Mark sets an upper limit on the amount of omega-3 fatty acids that can be present in the undisclosed 14% of fatty acids as 0.3% of total calories because the maximal amount permitted is 1.2% (FF 13–14). This fact and teaching of Mark was not addressed by any of the expert Declarations. Therefore, even if omega-3 fatty acids reach the maximal 1.2% of total calories permitted, the ratio of 4.9% omega-6 fatty acids to 1.2% omega-3 fatty acids exceeds 4:1, the ratio required by claim 65. Moreover, even if the omega-6 fatty acids reach the maximal 6% of total calories permitted (FF 13), the total grams of omega-6 fatty acids in a 1,000 mL dose would not exceed 40 grams as required by claim 65 (FF 14).

Therefore, when the teachings of Mark are considered in their entirety, we agree with the Examiner that the preponderance of the evidence supports the Examiner's finding that Mark anticipates the claimed 4:1 ratio of omega-6 to omega-3 fatty acids (FF 13, 14, 16).

Intermixture from different sources

Appellant contends that Mark does not teach a "disclosure of 'an intermixture of lipids [fatty acids] from different sources' in light of the lexicography of Appellant's specification" (App. Br. 44).

We do not find this argument persuasive because "different sources" is a product-by-process limitation. As discussed above, the patentability of a product-by-process claim is not dependent on process limitations. *See In re Thorpe*, 777 F.2d at 697. Here, the sources represent process limitations that have not been shown to necessarily impose any structural limitations on the

claimed composition. Indeed, even if this limitation were given structural weight, column 6 of Mark teaches a formulation comprising a mixture of oils including canola, soy, and coconut oils that all have both omega-6 and omega-3 fatty acids (FF 16; *cf.* Rucker Decl. 4/30/15 ¶ 10) with a omega-6 to omega-3 fatty acid ratio of 5:1 (FF 16).

Omega-6 and Omega-3 amounts

Appellant contends that "[c]oncentration of total omega-6 and omega-3 fatty acids cannot be calculated because 14% of the fatty acids are missing. Thus, Mark et al. do not disclose omega-6 and omega-3 concentrations" (App. Br. 45).

We are not persuaded. As already discussed, the minimal and maximal amounts of omega-6 and omega-3 fatty acids were disclosed by Mark (FF 13) resulting in weight values of fatty acids that necessarily fall within the 4–75% range for omega-6 and 0.1–30% range for omega-3 fatty acids, because the undisclosed 14% of fatty acids in Mark cannot cause the omega-6 or omega-3 fatty acid amounts to increase above the 75% or 30% maximums. Indeed, even if the entire 14% was omega-6 fatty acid, the total omega-6 fatty acid amount would be 26.2% (12.2% shown in table 4 plus 14% undisclosed) and if the entire 14% was omega-3 fatty acid, the total omega-3 fatty acid amount would be 16.4% (2.4% shown in table 4 plus 14% undisclosed). However, Mark's teaching that omega-6 cannot exceed 6% of KCAL and omega-3 cannot exceed 1.2% of KCAL (FF 13) further constrains these amounts to necessarily fall within the claimed range.

Mark Operability

Appellant cites the Erickson Declaration, which states that "Mark et al is not a credible reference. The reference uses terms such as 'Total' and 'lipids' negligently . . . . A practitioner using Mark et al. will not know what omega-6 to omega-3 ratios to use in total lipids and how much omega-6 and omega-3 to put into Mark et al formulations" (Erickson Decl. 3/31/15 ¶ 16; *cf.* Rucker Decl. 4/30/15 ¶ 10 and Das Decl. 4/30/15 ¶ 10).

We have considered the Erickson, Rucker, and Das Declarations, but do not find them persuasive of inoperability of the Mark reference. Mark specifically teaches a 5:1 omega-6 to omega-3 ratio in column 6 and provides a specific composition including amounts of a large number of formulation components (FF 16). The concerns the Declarants raise regarding lipid amounts do not apply to the composition of column 6 which teaches specific amounts of canola, soy and coconut oils as well as milk fat and soy lecithin to add to the composition (FF 16). "Enablement of prior art requires that the reference teach a skilled artisan to make or carry out what it discloses in relation to the claimed invention." *In re Antor Media Corp.*, 689 F.3d 1282, 1290 (Fed. Cir. 2012). Here, Mark teaches the skilled artisan the specific amounts of each component required by the formulation (FF 16).

Appellant and Declarants have not provided evidence that undue experimentation would have been required to follow the instructions of Mark and formulate the composition of column 6 using the specifically disclosed oils along with sources for carbohydrates, protein, vitamins, minerals, and any other listed components.

Claim 130

Appellant contends that "the descriptive 'vitamin E-alpha/gamma less than 0.5% by weight of total lipids' is missing from Mark" (App. Br. 47).

The Examiner finds that "the 18 mg of generic 'vitamin E' in the Nutrient Composition of Mark existed is present at~ 0.047 % by weight of total lipids, which meets the limitation (less than 0.5% by weight) [of] Claim 130" (Ans. 60).

The Examiner's position is supported by the weight of the evidence. In the table at column 6, Mark teaches 28 IU of vitamin E (FF 16). 28 IU of vitamin E is an amount that converts to some value less than 28 mg, depending upon the specific form of vitamin E. With a total lipid amount of 38.5 g, the amount by weight of vitamin E is less than 28 mg/38,500 mg or 0.07 %, a value less than the required 0.5% of total lipids.

Dependent Claims

We recognize, but find unpersuasive, Appellant's arguments regarding claim 68 (App. Br. 48) because Mark teaches 33% lipid, which reasonably supports the Examiner's position in the absence of evidence to the contrary (FF 16). Claim 68 requires less than 25% calories from either milk or cheese, so if whey is different than milk and cheese as argued by Appellant, then the amount of whey is irrelevant because it is not specifically excluded by claim 68.

We recognize, but find unpersuasive, Appellant's arguments regarding claim 69 (App. Br. 48) because claim 69 only requires that "one or more of the following apply," not that all of the following conditions apply. Thus, while Appellant is correct that the zinc level in Mark exceeds that

permitted by claim 69(vi), the vitamin C level in Mark is 100 mg (FF 16), less than the 400 mg required by claim 69(vi) and thereby satisfying the claim requirement for "one or more of the following" (*see* Ans. 62).

We recognize, but find unpersuasive, Appellant's argument regarding claim 73 (App. Br. 49) because the claim imposes no specific structural requirement on the formulation, and the "when the formulation is provided" limitation represents an intended use. However, a "mere statement of a new use for an otherwise old or obvious composition cannot render a claim to the composition patentable." *In re Zierden*, 411 F.2d 1325, 1328 (CCPA 1969).

We recognize, but find unpersuasive, Appellant's argument regarding claim 77 (App. Br. 49) because the composition of Mark may be administered in one-part as a feeding formula for any desired period of time (FF 9, 15).

We recognize, but find unpersuasive, Appellant's argument regarding claim 78 (App. Br. 49) because Appellant provides no evidence demonstrating that the delivery of omega-3 or omega-6 fatty acids is not gradual or steady. *See In re Best*, 562 F.2d 1252, 1255 (CCPA 1977) ("Where, as here, the claimed and prior art products are identical or substantially identical . . . the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product.").

We recognize, but find unpersuasive, Appellant's argument regarding claim 83 (App. Br. 49) because only one of the four recited conditions need apply and Mark teaches elements (i) and (ii) of claim 83 (FF 16).

We recognize, but find unpersuasive, Appellant's argument regarding claims 92, 93, and 95 (App. Br. 49) because Mark teaches 4.7 g of omega-6 fatty acids that represents 4.9% total calories and maximally 6% of total calories and therefore less than 6 g total (FF 13–14). These values fall within those required by claims 92 and 93, and the 0.9 g amount of omega-3 fatty acids falls within the range required by claim 95, even if the KCAL value is increased to the 1.2% maximum suggested by Mark (FF 13–14).

We recognize, but find unpersuasive, Appellant's argument regarding claim 96 (App. Br. 50) because Mark teaches the presence of additional nutrients (FF 16) and Appellant provides no evidence that the formulation in column 6 of Mark does not inherently satisfy the requirement of claim 96. *Best*, 562 F.2d at 1255.

We recognize, but find unpersuasive, Appellant's argument regarding claim 98 (App. Br. 50) because it represents intended uses of the formulation. *Zierden*, 411 F.2d at 1328. No specific structural limitations are imposed by claim 98.

We recognize, but find unpersuasive, Appellant's argument regarding claim 100 (App. Br. 50) for two reasons. We agree with the Examiner that "Mark teaches TOTAL fatty acids, explicitly teaches TOTAL mono and polyunsaturated fatty acids and thus allows for calculation of the ratio that meets the claim limitation" (Ans. 63). In addition, we note that whether the entire 14% was added to total fatty acids or to monounsaturated fatty acids, the resultant values would fall within the range of 1:1 to 15:1, the ratio required by claim 100.

We recognize, but find unpersuasive, Appellant's argument regarding claim 136 (App. Br. 50) because the "intended function of sucrose as recited in the claim is not accorded patentable weight" (Ans. 63). *Zierden*, 411 F.2d at 1328.

We recognize, but find unpersuasive, Appellant's argument regarding claim 137 (App. Br. 50) because Mark teaches pediatric patients (FF 9) which necessarily encompasses human infants and children.

We recognize, but find unpersuasive, Appellant's argument regarding claims 142 and 144 (App. Br. 50–51) because Mark clearly teaches lipids from canola, soy, and coconut oils, which clearly represent different sources (FF 16).

Appellant also lists claims 61, 68, 69, 74, 82, 94, 97, 102, 107, 142, and 144 but provides no specific arguments. "A statement which merely points out what a claim recites will not be considered an argument for separate patentability of the claim." 37 C.F.R. § 41.37(c)(1)(iv). Here, Appellant does not even identify the claim recitations and provides no specific argument that Mark does not anticipate these claims.

Conclusion of Law

The preponderance of the evidence in the record supports the Examiner's conclusion that Mark anticipates the claims.

C. 35 U.S.C. § 102(b) over Olives and "Olives Nutrient Analysis"

The Examiner finds that the "lipid-formulation of 'Olives' is clearly edible and . . . . The intended use of the olive/brine formulation is to be

eaten" (Ans. 66). The Examiner finds that "Olive Nutrient Analysis" ("ONA") teaches that:

> 1.00 cup serving of black olives contains: 1) 1.14 g omega-6 fatty acids (7.94% by weight of total lipids) and 0.09 g omega-3 fatty acids (0.63% by weight of total lipids); instant Claims 65, 83, 92, 93, 118 and 129), 2) olive oil (instant Claim 61; embodiment (iii)), 3) linoleic acid (18:2) (instant Claim 52), 4) carbohydrates and protein (instant Claim 67), 5) a source of fiber (instant Claim 69), 6) a ratio of total fatty acids:monounsaturated fatty acids= 1.35:1 (14.35/10.60) (instant Claim 100), 7) 154.56 calories, of which 129.19 of the calories (83.5%) are from fat, (as such, the diet (1.00 cup of olives) supplies 83.5% of the diet's fat calories; instant Claim 74), 8) 14.35 g of fatty acids (expressed as "Total Fat"; instant Claim 94), and, 9) 2.9% calories from 1.13 g protein (i.e. "less than 75% are from legumes and "less than 15% . . . from other sources"; instant Claim 68).

(Ans. 68–69).

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that "Olives" as evidenced by "Olive Nutrient Analysis" anticipates the claims?

Findings of Fact

17. "Olives" teaches "[s]ome of the many available delicious varieties of olives include Moroccan oil-cured, Kalamata, Nicoise, Picholine and Manzanilla" ("Olives" 2–3).

18. "Olives Nutrient Analysis" teaches "Olives, black, canned" with a serving size of "1.00 cup (134.40 g)" that contains

Olives, black, canned (Note: "--" indicates data unavailable)		
1.00 cup (134.40 g)	GI: very low	
BASIC MACRONUTRIENTS AND CALORIES		
nutrient	**amount**	**DRI/DV (%)**
Protein	1.13 g	2.26
Carbohydrates	8.41 g	3.74
Fat - total	14.35 g	--
Dietary Fiber	4.30 g	17.20
Calories	154.56	8.59

INDIVIDUAL FATTY ACIDS		
nutrient	**amount**	**DRI/DV (%)**
Omega-3 Fatty Acids	0.09 g	3.75
Omega-6 Fatty Acids	1.14 g	

resulting in ~ 12:1 ratio of omega-6 to omega-3 ("Olives Nutrient Analysis" 1, 5).

Analysis

We adopt the Examiner's findings of fact and reasoning regarding the scope and content of "Olives" and "Olive Nutrient Analysis" (Ans. 65–72; FF 17–18) and agree that the claims are anticipated. We address Appellant's arguments below.

Appellant contends that "[t]here is no suggestion in Olives or ONA regarding an intermixture of lipids [fatty acids] from different varieties or sources" (App. Br. 53).

We do not find this argument persuasive for the reasons extensively addressed above. To briefly recap, the limitation to "intermixture of lipids from different sources" is a product-by-process limitation that imposes no specific structure on the lipid-containing formulation. *Thorpe*, 777 F.2d at 697.

Appellant contends that "it is improper to construe the feature 'intermixtures of lipids [fatty acids] from different sources' as product-by-process" (App. Br. 55).

We do not find this argument persuasive because Appellant has not demonstrated a difference between a can of black olives composed of the Kalamata variety from a can of black olives of the Manzanilla variety. This is the essence of product-by-process because the final formulation differs only in the process by which it is made, but contains the same omega-3 to omega-6 fatty acid ratio in the same amounts as required by the claims.

Appellant contends that "the webpages that disclose 'Olives' and 'ONA' teach mixtures of foods, including lipids from different sources, wherein overall ratio of omega-6 to omega-3 is around 2:1" (App. Br. 55). Appellant contends that "[t]hree skilled persons have testified, 'This teaching is applicable to all food mixtures taught by the site.' See paragraph [0010] of the Rucker, Rustagi, and Das declarations submitted on October 1, 2014" (App. Br. 55).

We are not persuaded. The teaching of "WHFoods"[13] is that the "ideal ratio of omega-3 to omega-6 is not known, but is estimated to be around 1:2; whereas, the current ratio in the typical American diet is more like 1:25" ("WHFoods" 9). This is not relevant to the amounts of omega-3 and omega-6 fatty acids in a specific food such as a serving of olives. Further, the Declarations simply contend that "authoritative guidelines do

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[13] WHFoods: A New Way of Looking at Proteins, Fats and Carbohydrates, http://web.archive.org/web/20070104020351/ http://whfoods.com/gen page. php?tname=faq&dbid=7 (accessed Apr. 12, 2014).

not recognize the significance of 'total lipids' as a category" (Rucker Decl. 4/30/15 ¶ 13; *cf.* Erickson Decl. 3/31/15 ¶ 20; Das Decl. 4/30/15 ¶ 13; Rustagi Decl. 9/29/14[14] ¶ 10), but provide no evidence that olives in cans for consumptions lack the required omega-3 and omega-6 fatty acids in the required ratio.

Appellant contends that "the practitioner is neither motivated nor taught to modify ONA ... in order to obtain total lipids or a ratio of omega-6 and/or omega-3 to total lipids.'" (App. Br. 56).

We are not persuaded because the rejection is for anticipation, not obviousness. The Examiner cites "Olive Nutrient Analysis" to evidence that olives contain 14.35 g total fat composed in part of 0.09 g omega-3 fatty acids and 1.14 g of omega-6 fatty acids, "resulting in ~ 12:1 ratio of omega-6 to omega-3" (FF 18). Appellant provides no evidence in rebuttal, nor do the Declarants specifically contest the composition disclosed by "Olive Nutrient Analysis."

Claim 130

Appellant contends that "Claim 130 requires presence of additional features that add to the novelty over 'Olives' and 'ONA'" (App. Br. 57).

We are not persuaded because the Examiner finds that "it is noted that Olives contains 4.03 mg vitamin E (less than 0.5% total lipids)" (Ans. 89), a finding that is not rebutted by Appellant.

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[14] Declaration of Dr. Pradip K. Rustagi, dated Sept. 29, 2014.

Dependent Claims

We recognize, but find unpersuasive, Appellant's arguments regarding claim 67 (App. Br. 58) because "Olive Nutrient Analysis" teaches that olives contain protein and carbohydrates (FF 18).

We recognize, but find unpersuasive, Appellant's arguments regarding claim 68 (App. Br. 58) because "protein in olives and walnuts . . . is less than 75% are from legumes, and less than 15% are from other sources" (Ans. 89). That is, the protein in olives is not derived from the prohibited sources of claim 68.

We recognize, but find unpersuasive, Appellant's argument regarding claims 73 and 74 (App. Br. 58) because the claims impose no specific structural requirement on the formulation, and the "when the formulation is provided" or "supplies 60–90% of a diet's fat calories" limitations represent intended uses. However, a "mere statement of a new use for an otherwise old or obvious composition cannot render a claim to the composition patentable." *Zierden*, 411 F.2d at 1328.

We recognize, but find unpersuasive, Appellant's argument regarding claim 77 (App. Br. 58) because the olive composition may be administered in one-part "serving size" for any desired period of time (FF 18).

We recognize, but find unpersuasive, Appellant's argument regarding claim 78 (App. Br. 59) because Appellant provides no evidence demonstrating that the delivery of omega-3 or omega-6 fatty acids is not gradual or steady. *See Best*, 562 F.2d at 1255 ("Where, as here, the claimed and prior art products are identical or substantially identical . . . the PTO can

require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product.").

We recognize, but find unpersuasive, Appellant's argument regarding claims 96 and 97 (App. Br. 59) because "Olive Nutrient Analysis" teaches the presence of additional nutrients (FF 18) and "Olives" teaches that "olives contain a variety of beneficial active phytonutrient compounds including *polyphenols*" (Olives 1). Appellant provides no evidence that the formulation does not inherently satisfy the functional requirements of claims 96 and 97. *Best*, 562 F.2d at 1255.

We recognize, but find unpersuasive, Appellant's argument regarding claim 98 (App. Br. 59) because it represents intended uses of the formulation. *Zierden*, 411 F.2d at 1328. No specific structural limitations are imposed by claim 98.

We find Appellant's argument regarding claim 136 (App. Br. 59) persuasive because the Examiner has not established the presence of any of the listed carriers in olives.

We recognize, but find unpersuasive, Appellant's argument regarding claim 137 (App. Br. 59) because olives may be consumed by adults.

We recognize, but find unpersuasive, Appellant's argument regarding claim 142 (App. Br. 60) because the olives contain fatty acids that are necessarily either in the free or ester form.

We recognize, but find unpersuasive, Appellant's argument regarding claim 144 (App. Br. 60) that olives are not an "intermixture" for the reasons already given above.

Appellant also lists claims 61, 68, 69, 95, 102, 107, 142, and 144 but provides no specific arguments. "A statement which merely points out what a claim recites will not be considered an argument for separate patentability of the claim." 37 C.F.R. § 41.37(c)(1)(iv). Here, Appellant does not identify the claim recitations and provides no specific arguments that "Olives" does not anticipate these claims.

Conclusion of Law

The evidence of record supports the Examiner's conclusion that "Olives" as evidenced by "Olive Nutrient Analysis" anticipates the claims.

D. 35 U.S.C. § 102(b) over Walnuts and "Walnut Nutrient Analysis"

The Examiner finds that "'Walnuts' teaches . . . amounts and health ratings of certain nutrients present in a 0.25 cup serving of walnuts" (Ans. 73). The Examiner finds that "a 0.25 cup serving of walnuts contain: 1) 9.52 g omega-6 fatty acids (54% by weight of total lipids) and 2.27 g omega-3 fatty acids (13.9 % by weight of total lipids)" (Ans. 77).

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that "Walnuts" as evidenced by "Walnut Nutrient Analysis" anticipates the claims?

Findings of Fact

19. Walnut teaches "[w]alnuts are a delicious way to add extra nutrition, flavor and crunch to a meal" and that "several polyphenolic compounds [are] found in walnuts" (Walnut 1). Walnut teaches that "three of the main types of walnuts consumed are the English (or Persian) walnut, *Juglans regia;* the Black walnut, *Juglans nigra;* and the White (or butternut) walnut, *Juglans cinerea*" (Walnut 4).

20. "Walnut Nutrient Analysis" teaches 25 g serving size contains

Basic Components		
nutrient	amount	%DV
calories	163.50	
calories from fat	146.72	
calories from saturated fat	13.78	
protein	3.81 g	
carbohydrates	3.43 g	
dietary fiber	1.68 g	6.72
soluble fiber	0.40 g	
insoluble fiber	0.81 g	
sugar - total	0.65 g	
monosaccharides	0.09 g	
disaccharides	0.53 g	
other carbs	1.30 g	
fat - total	16.30 g	
saturated fat	1.53 g	
mono fat	2.23 g	
poly fat	11.79 g	
trans fatty acids	0.00 g	
cholesterol	0.00 mg	
water	1.02 g	
ash	0.45 g	

Other Fats		
nutrient	amount	%DV
omega 3 fatty acids	2.27 g	90.80
omega 6 fatty acids	9.52 g	

("Walnut Nutrient Analysis" 1, 3).

Analysis

We adopt the Examiner's findings of fact and reasoning regarding the scope and content of "Walnuts" and "Walnut Nutrient Analysis" (Ans. 73–83; FF 19–20) and agree that the claims are anticipated. We address Appellant's arguments below.

Appellant contends that "there is no suggestion in 'Walnuts' or 'WNA' regarding an "intermixture of lipids [fatty acids] from different varieties or sources'" (App. Br. 62).

We do not find this argument persuasive for the reasons extensively addressed above. To briefly recap, the limitation to "intermixture of lipids

from different sources" is a product-by-process limitation that imposes no specific structure on the lipid-containing formulation. *Thorpe*, 777 F.2d at 697.

Appellant contends that "the webpages that disclose 'Walnuts' and 'WNA' teach mixtures of foods, including lipids from different sources, wherein overall ratio of omega-6 to omega-3 is 'around 2:1'" (App. Br. 62).

We do not find this argument persuasive because "Walnut Nutritional Analysis" expressly teaches that a serving of walnuts contains 9.52 g omega-6 fatty acids and 2.27 g omega-3 fatty acids for a ratio of 4.2:1, satisfying the requirements of claim 65.

Claims 91 and 130

Appellant contends that "Claims 91 and 130 require presence of additional features that add to the novelty over 'Walnuts' and 'WNA'" (App. Br. 63).

We are not persuaded because Walnuts teaches the presence of polyphenols (FF 19), one of the optional nutrients required by claims 91 and 130.

Dependent Claims

We recognize, but find unpersuasive, Appellant's arguments regarding claim 67 (App. Br. 64) because "Walnut Nutrient Analysis" teaches that olives contain protein and carbohydrates (FF 20).

We recognize, but find unpersuasive, Appellant's arguments regarding claim 68 (App. Br. 64) because "protein in olives and walnuts . . . is less than 75% are from legumes, and less than 15% are from other

sources" (Ans. 89). That is, the protein in walnuts is not derived from the prohibited sources of claim 68.

We recognize, but find unpersuasive, Appellant's argument regarding claims 73 and 74 (App. Br. 64) because the claims impose no specific structural requirement on the formulation, and the "when the formulation is provided" or "supplies 60–90% of a diet's fat calories" limitations represent intended uses. However, a "mere statement of a new use for an otherwise old or obvious composition cannot render a claim to the composition patentable." *Zierden*, 411 F.2d at 1328.

We recognize, but find unpersuasive, Appellant's argument regarding claim 77 (App. Br. 64) because the walnut composition may be administered in one-part "serving size" for any desired period of time (FF 20).

We recognize, but find unpersuasive, Appellant's argument regarding claims 78 and 124 (App. Br. 64) because Appellant provides no evidence demonstrating that the delivery of omega-3 or omega-6 fatty acids is not gradual or steady. *See Best*, 562 F.2d at 1255 ("Where, as here, the claimed and prior art products are identical or substantially identical . . . the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product.").

We recognize, but find unpersuasive, Appellant's argument regarding claims 96 and 97 (App. Br. 64–65) because "Walnut Nutrient Analysis" teaches the presence of additional nutrients (FF 20) and "Walnuts" teaches that "several polyphenolic compounds [are] found in walnuts" (FF 19). Appellant provides no evidence that the formulation does not inherently

satisfy the functional requirements of claims 96 and 97. *Best*, 562 F.2d at 1255.

We recognize, but find unpersuasive, Appellant's argument regarding claims 98, 102, 118, and 122 (App. Br. 65) because the arguments rely upon intended uses of the formulation. *Zierden*, 411 F.2d at 1328. No specific structural limitations are imposed by these claims.

We recognize, but find unpersuasive, Appellant's argument regarding claim 128 (App. Br. 65) because the claim is a product-by-process claim and Appellant has not shown any structural differences resulting from the process. *Thorpe*, 777 F.2d at 697.

We recognize, but find unpersuasive, Appellant's argument regarding claims 136 and 139 (App. Br. 65) because "Walnut Nutrient Analysis" teaches that walnuts contain sugars including disaccharides as required by the claims (FF 20).

We recognize, but find unpersuasive, Appellant's argument regarding claims 137 and 140 (App. Br. 66) because walnuts may be consumed by adults.

We recognize, but find unpersuasive, Appellant's argument regarding claims 142 and 144 (App. Br. 66) that walnuts are not an "intermixture" for the reasons already given above.

Appellant also lists claims 61, 68, 69, 82, 107, 118, 120, 135, 138, and 141–145 but provides no specific arguments. "A statement which merely points out what a claim recites will not be considered an argument for separate patentability of the claim." 37 C.F.R. § 41.37(c)(1)(iv). Here,

Appellant does not identify the claim recitations and provides no specific arguments that "Walnuts" does not anticipate these claims.

Conclusion of Law

The evidence of record supports the Examiner's conclusion that "Walnuts" as evidenced by "Walnut Nutrient Analysis" anticipates the claims.

SUMMARY

In summary, we affirm the rejection of claims 52, 61, 64, 65, 67–69, 73–75, 77, 78, 80, 82, 83, 90–102, 107, 116–122, 124, and 128–145 under 35 U.S.C. § 101 as directed to non-statutory subject matter.

We affirm the rejection of claims 52, 61, 64, 65, 67–69, 73, 75, 77, 78, 80, 83, 90, 92–96, 98, 100, 129–131, 133–137, 142, and 144 under 35 U.S.C. § 102(b) as anticipated by Mark.

We affirm the rejection of claims 52, 61, 64, 65, 67–69, 73–75, 77, 78, 80, 82, 83, 90, 92–94, 96–98, 100, 129–131, 133, 137, 142, and 144 under 35 U.S.C. § 102(b) as anticipated by Olives as evidenced by "Olives Nutrient Analysis."

We reverse the rejection of claim 136 under 35 U.S.C. § 102(b) as anticipated by Olives as evidenced by "Olives Nutrient Analysis."

We affirm the rejection of claims 52, 61, 64, 65, 67–69, 73–75, 77, 78, 80, 83, 90–101, 116–118, 120–122, 128–140, and 141–145 under 35 U.S.C. § 102(b) as anticipated by Walnuts as evidenced by "Walnut Nutrient Analysis."

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

ANNEX H:

Annotated Opinion of the United States Court of Appeals for the Federal Circuit dated March 16, 2018

Note: Emphasis in the body and annotations in side columns are added by the Appellant. The #signs refer to points of law or fact overlooked or misapprehended by the panel and discussed in the petition.

NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

IN RE: URVASHI BHAGAT,
Appellant

2016-2525

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. 12/426,034.

Decided: March 16, 2018

URVASHI BHAGAT, Palo Alto, CA, pro se.

NATHAN K. KELLEY, Office of the Solicitor, United States Patent and Trademark Office, Alexandria, VA, for appellee Andrei Iancu. Also represented by THOMAS W. KRAUSE, AMY J. NELSON.

Before NEWMAN, O'MALLEY, and TARANTO, *Circuit Judges.*

NEWMAN, *Circuit Judge.*

Urvashi Bhagat ("the Applicant") appeals the decision of the Patent Trial and Appeal Board ("the Board") affirming the examiner's rejection of claims 52, 61, 64, 65, 67–69, 73–75, 77, 78, 80, 82, 83, 90–102, 107, 116–122, 124,

and 128–145 of U.S. Patent Application No. 12/426,034 ("the '034 application").[1] We affirm the Board's decision.[2]

BACKGROUND

The '034 application is directed to lipid-containing compositions comprising omega-6 and omega-3 fatty acids. The '034 application states that dietary deficiency or imbalance of these fatty acids may lead to a variety of illnesses, and that omega-6 and omega-3 fatty acids are naturally occurring in oils, butters, nuts, and seeds. The '034 application claims a range and ratios of these fatty acids and other limitations. Application claim 65 is the broadest claim:

> 65. A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids from different sources, and wherein
>
> > (1) omega-6 fatty acids are 4–75% by weight of total lipids and omega-3 fatty acids are 0.1–30% by weight of total lipids; or
> >
> > (2) omega-6 fatty acids are not more than 40 grams.

Other claims add specificity of amounts or ratios, additional ingredients, sources of the lipids, and delivery methods. The examiner held all of the claims unpatenta-

Panels has failed to consider full background--the opposite teachings, mass confusion, public suffering--and advancement potential in the art and extremely important inventive concept in the claimed inventions. Prior art overwhelmingly teaches omega-6 to omega-3 ratio <4:1 and omega-6 <10% of total fat and <6.67g/day and and teaches suppression of omega-6, which is deleterious. Appellant submitted 14 pages of BACKGROUND because of mass confusion in the art UBBr3-9, 54, 79-80, and UBRBr1-4, calling attention to numerous scientific publications, PHOSITA testimony, and the cited art as evidence of opposite teachings in the art and public suffering in 1421-page Joint Appendix, which the panel has overlooked. See #18 and pages 18-23 in the Petition for Rehearing.

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[1] *In re Bhagat*, Appeal No. 2016–004154 (P.T.A.B. Apr. 15, 2016) ("Board Op.").

[2] Applicant's motions to expedite are denied as moot.

ble as directed to products of nature, and also held most claims unpatentable as anticipated.

The Board sustained the rejection of the claims, leading to this appeal.

DISCUSSION

PANEL HAS FAILED TO CONSTRUCT CLAIMS DE NOVO AS PER LAW, AND OVERLOOKED UBBR40-49 WHERE CLAIM CONSTRUCTION ASSISTANCE WAS PROVIDED PROACTIVELY.

On review of the Board's decision on an examiner's rejection, the Board's legal determinations receive de novo review, and the Board's factual findings are reviewed for support by substantial evidence in the examination record. *In re Am. Acad. of Sci. Tech Ctr.*, 367 F.3d 1359, 1363 (Fed. Cir. 2004). Claims in pending applications receive their broadest reasonable interpretation during examination, for adjustment of claim scope or clarification of meaning may be achieved by amendment during examination.

Nothing in this case implicates deference to fact finding. It is simply a matter of reading the publications. Claims and prior art construction, and eligibility determinations is a matter of law that the panel has a duty to review DE NOVO without deference. Excising limitations from claims is simply not reasonable. See #1-9, 16, and 19.

I

ANTICIPATION

A. The Mark reference

The Board affirmed the examiner's rejection of claims 52, 61, 64, 65, 67–69, 73, 75, 77, 78, 80, 83, 90, 92–96, 98, 100, 129–131, 133, 135–137, 142 and 144 on the ground of anticipation by U.S. Patent No. 5,549,905 ("Mark"). Mark describes a nutritional composition for pediatric patients, including a protein source, carbohydrate source, and lipid source containing omega-6 and omega-3 fatty acids in a ratio of "approximately 4:1 to 6:1." Mark, col. 2, ll. 32–38; col. 4, ll. 21–23. Mark states that the omega-6 fatty acid "is present in a range of approximately 4–6% of the total calories" of the pediatric composition, and the omega-3 fatty acid "is preferably present in the range of approximately 0.8–1.2% of the total calories." *Id.* at col. 4, ll. 27–31. Mark describes a specific composition containing 38.5 grams of total lipids, *id.* at col. 6, l. 9, administered intra-

There is no implication of deference to PTAB's findings here, this is a question of interpretation of prior art, which is a legal question that panel has to review DE NOVO as per law, and it simply requires reading Mark. Panel failed to interpret Mark's "lipids" de novo as per law, which in Mark means oils, which contain non-lipids. Mark discloses "omega-3 to omega-6 fatty acid ratio of approximately 4:1 to 6:1" in col.2.ll.37-38, i.e., "omega-6 to omega-3 fatty acid ratio of approximately 1:4 to 1:6" and SOURCE of omega-6 (e.g. an oil) is present at 4-6% of calories NOT omega-6 is present at 4-6% of calories in col.4.ll.27-31.
See #9.

venously in a "typical feeding regimen" of "50 mL/hour for 20 hours/day," *id.* at col. 5, ll. 7–8.

The Board agreed with the examiner that Mark discloses minimum and maximum amounts of omega-6 and omega-3 fatty acids within the claimed range, and also discloses a mixture of several types of oils as fatty acid sources. The Applicant argues that Mark does not "unequivocal[ly]" disclose the claimed omega-6 to omega-3 ratio because Mark does not clearly state whether its compositions are total omega-6 and omega-3 acids, or only alpha-linolenic and linoleic acids. The Board found that Mark expressly discloses an omega-6 to omega-3 fatty acid ratio of 5:1; Mark, col. 6, l. 15; which is within the ratios in all of the '034 application claims. Board Op. at *19.

The Applicant also argues that Mark does not meet the "dosage" limitation of claim 65 because Mark discloses concentrations of nutrients, rather than a dosage of omega-6 and omega-3 fatty acids. Responding to this argument, the Board found that Mark's "typical feeding regimen" of "50 mL/hour for 20 hours," a total of 1,000 mL/day, meets the claim 65 "dosage," for Mark's daily dosage may include 1,000 mL, as the table in column 4 refers to g/1,000 mL, teaching the daily amount fed to a child. Board Op. at *18. This finding is supported in the record, as is the Board's resulting finding of anticipation of claims 65, 92–93, and 95 based on Mark's feeding regimen within the dosage stated in these claims.

The Applicant argues that even if the broadest claims are deemed anticipated by Mark, the other claims are not anticipated. The Applicant argues that Mark teaches a composition for children ages 1–10, and does not anticipate claim 137 which states "the formulation is for a human infant, or adult." The Board found this argument did not distinguish claim 137 because "Mark teaches pediatric patients which necessarily encompasses human

PHOSITA have testified that Mark does not enable dosage of omega-6 and omega-3. See #10.

This is hindsight optimization. Mark did not disclose min/max amounts of n6/n3. See #9.

Mark does not necessarily function as "intermixture of lipids from different sources." PHOSITA have testified on record that Mark's Table in col. 6 is NOT operable. See #11.

Panel has misapprehended, PTO did not reject claims 82, 91 and dependent claims under Mark by PTO. See #12.

Under anticipation law Mark has to necessarily function and enable dosage of omega-6 and omega-3, "MAY" is not sufficient, specially in light of the fact that temporal art does not understand correct "dosage of omega-6." Panel disregarded PHOSITA testimony. See #10

Panel failed to address claims 129 and 130 and several others claims under Mark. See #12.

infants and children." Board Op. at *26. We discern no error in the finding that claim 137, which includes "human infants," is anticipated by Mark's reference to children ages 1–10.

Panel has overlooked that Mark has NOT taught and enabled dosage, which is different among children 1-10. See #10.

Board's Op at 11 pertains to eligibility under § 101 not to Mark, panel is confusing § 101 with § 102.

The Board received argument of the general unpredictability of components of natural products, and deemed this argument irrelevant because "the Examiner relies upon evidence of particular compositions of walnut oil or olive oil that satisfy the requirements of claim 65." Board Op. at *11. This is a correct application of the law of anticipation, for compositions containing the components and ratios in claim 65 are shown in Mark for uses that include the pediatric use described in Mark. The Applicant's claims are all directed to formulations and compositions, not to any asserted new use.

PANEL FAILS TO CITE ANY LAW WHY INDEPENDENT CLAIMS ARE ANICIPATED BY MARK.

NO. In Nidec Judge Taranto ruled, "[anticipation law] does not permit [] to fill in missing limitations simply because a skilled artisan would immediately envision them." Here PHOSITA do not even envision the claimed limitations. See #9-12. "Dosage" IS A NEW USE.

The Board also found that while "casing" and "dosage" are not expressly defined, the specification states that any "orally accepted form" of delivery is within the scope of the claims. Board Op. at *9. The specification states that "the compositions comprising the lipid formulation disclosed herein may be administered to an individual by any orally accepted form." J.A. 65 ¶34. The Board found that the "casing" and "dosage" terms do not impart patentability to the claimed compositions, and we agree, for the specification states that these claim elements are not limiting, and does not describe any assertedly novel characteristics of these components or their formulations.

"ANY ORALLY ACCEPTED FORM" IN SPECEFICATION REFERS TO TYPE OF FOOD NOT AMOUNT OR "DOSAGE." #2.

A. Specification does NOT state "these claim elements" are not limiting. Specification provides five tables with "dosages" by age and gender and 17 examples where it repeatedly emphasizes dosage of omega-6 is critical and prior art has failed to understand dosage and dose effect (changing effect by dose level) of omega-6. Under such disclosure there is NO JUSTIFICATION for alleging "dosage" or "casings providing controlled delivery" are not limiting in Specification.

B. In prosecution the inventor and PHOSITA gave testimony to the interpretation of "dosage" and "casings providing controlled delivery".

See #2-4.

Frankly, the allegations are so improper that they are unfitting for 2nd highest seat of justice in USA, the "most advanced country" in the world.

Panel has overlooked that Claim 78 recites "omega-3 withdrawal … increase is gradual" the limitations are missing from Mark. Appx7707, Appx7893. "[anticipation law] does not permit [] to fill in missing limitations simply because a skilled artisan would immediately envision them." Nidec.

The Applicant also argues that Mark does not teach "steady delivery" as required by claim 78. Claim 78 states "the formulation provides gradual and/or steady delivery so that any omega-3 withdrawal is gradual, and/or any omega-6 and/or other fatty acid increase is gradual." The Board found that claim 78 does not recite a patentably significant difference from Mark's typical feeding regimen of 50 mL/hour for 20 hours. Board Op. at *24. The Applicant does not provide any distinction in claim 78 from

Mark's typical feeding regimen, and does not overcome the Board's finding of prima facie anticipation of claim 78 by Mark.

PANEL HAS OVERLOOKED TO REVIEW AT LEAST CLAIMS 129, 130, 68, 69, 73, 96, 98, 100, 142, 144 UNDER MARK. SEE #12 AND UBBR67-68.

The PTO concedes that the Board incorrectly included claim 134 in the claims found to be anticipated by Mark. However, the PTO argues that claim 134 is anticipated by the Walnut Nutrient Analysis on the same basis as for the other claims, and also is unpatentable under Section 101.

B. *The Olive and Walnut Nutrient Analyses*

It is improper to even discuss olives and walnuts. OPINION SHOULD JUST SAY:
A. olives and walnuts were disclaimed in prosecution; see #13; and
B. neither is "formulation" let alone "intermixture of lipids from different sources" in "casings providing controlled delivery of the formulation to a subject;" see #14; and
C. PHOSITA have testified that the references do not teach "dosage" of omega-6/omega-3; see #14. THEN FURTHER DISCUSSION IS NOT NEEDED.

The examiner rejected claims 52, 61, 64, 65, 67–69, 73–75, 77, 78, 80, 82, 83, 90, 92–94, 96–98, 100, 129–131, 133, 136, 137, 142, and 144 as anticipated by the nutrient profile of a serving of olives, whose fatty acid composition is shown in "Olive Nutrient Analysis," http://web.archive.org/web/20060314112106/http://www.whfoods.com/genpage.php?tname=nutrientprofile&dbid=111 (Mar. 14, 2006).

The Olive Nutrient Analysis describes a one cup serving of olives as containing omega-6 and omega-3 fatty acids in a 12:1 ratio. The Board agreed with the examiner's finding that the Olive Nutrient Analysis shows a serving size within the claimed dosage, and shows that olives contain a combination of lipids within the scope of the claims. The Olive Nutrient Analysis shows 1.14 grams of omega-6 fatty acids in a one cup serving, which is within the limitation in all the claims that "omega-6 fatty acids are not more than 40 grams."

Discussion of Claim 136 is insincere and deflects the point above.

The Board affirmed the examiner's rejection except for claim 136, which the Board reversed with respect to the Olive Nutrient Analysis. Board Op. at *38. The Board held that the examiner had not established that olives contain the claimed combination with "one or more carriers selected from starches, sugars, granulating agents, binders and disintegrating agents." Board Op. at *13–14, 32. However, the Board sustained the examiner's rejection of claim 136 with respect to the Walnut Nutrient

Analysis as that reference "teaches that walnuts contain sugars including disaccharides as required." Board Op. at *37. On this appeal the PTO does not discuss claim 136 with regard to olives, but argues that claim 136 is anticipated by the Walnut Nutrient Analysis and invalid under Section 101.

The examiner rejected claims 52, 61, 64, 65, 67–69, 73–75, 77, 78, 80, 83, 90–101, 116–118, 120–22, 124, 128–140, and 141–145 as anticipated by the nutrient profile of a serving of walnuts as reported in the Walnut Nutrient Analysis, http://web.archive.org/web/20061109221127/http://whfoodw.com/genpage/php?tname=nutrientprofile&dbid=132 (Nov. 9, 2006). The Walnut Nutrient Analysis states that a 25 gram serving of walnuts contains omega-6 and omega-3 fatty acids in a 4.2:1 ratio. The Walnut Nutrient Analysis shows 9.52 grams of omega-6 fatty acids in a quarter-cup serving, which is within the limitation that "omega-6 fatty acids are not more than 40 grams." The Board agreed with the examiner that the reference's serving size of walnuts contains a dosage of lipids within the scope of the claims. The Board affirmed all of the claim rejections on this Walnut reference.

See points made above under #13-14. Bottom line is that olives/ walnuts were disclaimed and olives/walnuts do not disclose "intermixture of lipids from different sources" and do not necessarily function in accordance with the claims. They teach random consumption of olives and walnuts and mixing them with foods to lower omega-6 to omega-3 ratio below 2:1. UBBr74.

PANEL ACKNOWLEDGES THAT APPLICANT DISCLAIMED SINGLE SOURCE SUCH AS OLIVES AND WALNUTS, THEN DISREGARDS THE UNDISPUTED FACT IN FURTHER ANALYSIS. #13.

The Applicant states that the Board erroneously ignored a prosecution disclaimer of all compositions containing products from single sources such as olives and walnuts. The Applicant points out that all the claims are directed to formulations containing mixtures of omega-6 and omega-3 fatty acids, and that the Walnut and Olive Nutrient Analyses do not describe the specific mixtures that limit all the claims; for example, the Claim 65 requirement that "omega-6 fatty acids are 4–75% by weight of total lipids and omega-3 fatty acids are 0.1–30% by weight of total lipids." The Applicant also argues that the total lipids in these formulations are not described in the Walnut and Olive Nutrient Analyses. The Board found that all of the rejected claims include fatty acid quantities and ratios within the "dosages" in the Nutrient Analysis

references. The Board's finding that the references' serving sizes of olives and walnuts meet the "dosages" in the claims is supported by substantial evidence in the record.

PHOSITA testimony disagrees that serving size in olives is a dosage. See #14.

The Applicant argues that a "serving" of olive oil or walnut oil, as reported in the Olive and Walnut Nutrient Analyses, is not a "dosage," but merely a way to measure nutrient density. The Board found that the Applicant's dosage is limited only in that the maximum content of omega-6 fatty acids is "not more than 40 grams," Claim 65, *ante*. The Board found that this is not a patentable distinction from the prior art, which shows omega-6 fatty acids in this range. We discern no error in this conclusion.

Claim 65 recites, "A lipid-containing formulation, comprising a dosage of omega-6 (main clause)… wherein …omega-6 fatty acids are not more than 40 grams (subordinate clause)." The panel divorced main clause from the subordinate clause. Disregarding context of surrounding words is simply NOT reasonable. Even without the subordinate clause, "dosage" in MAIN CLAUSE cannot be excized. #2-4, 7-8.

PANEL FAILS TO CITE ANY LAW WHY INDEPENDENT CLAIMS 65, 91, 129, AND 130 ARE ANICIPATED BY WEBOLIVES/ WEBWALNUTS.

The Board also considered the Applicant's separate arguments of patentability of several of the dependent claims. The Applicant argues that the Olive Nutrient Analysis does not show the vitamin E ratio in claim 130 ("vitamin E-alpha/gamma less than 0.5% by weight of total lipids"). However, the Board found that the Olive Nutrient Analysis states that the measured serving of olives contains 4.03 mg of "vitamin E alpha equiv" and 14.35 g of total fat (lipids). Board Op. at *30. These amounts are within the scope of claim 130. The Applicant does not show error in the Board's finding that the reference shows a Vitamin E presence within the claimed range.

References provide catalog of LARGE number of parts. Considering that relevance of total lipids in temporal art is not understood, part-to-part teaching is critical, which the references fail to provide. UBBr76; UBRBr30. #14.

For claims 67 and 68 the Board found that the protein in walnuts and olives meets the "protein source" designated in these claims. The Board found that the Walnut Nutrient Analysis includes protein and carbohydrates as recited in claim 67, and "the protein in walnuts is not derived from the prohibited sources of claim 68." Board Op. at *35–36. Claim 78 recites "steady" delivery, e.g., "[t]he formulation of claim 65, whereby the formulation provides gradual and/or steady delivery so that any

Panel has disregarded Appellant's rebuttal to Decision on claims 68, 73, 74, 77, 78, 96-98, 102, 107, 118, 119, 121, 122, 124, 128(1), 137, 140, 141. UBBr 76-77. Panel insincerely regurgitated PTAB Decision.

omega-3 withdrawal is gradual, and/or any omega-6 and/or other fatty acid increase is gradual." Claims 73, 74, 98, 118, 122, 137 and 140 add limitations directed to intended use. Claims 96 and 97 include limitations of additional nutrients and polyphenols.

The Board found that all of the additional limitations are known aspects used in known conditions, as shown in Mark or in the Olive or Walnut Nutrient Analysis. These findings are supported by substantial evidence in the cited references. The examiner's prima facie case of anticipation by these known fatty acid compositions and uses was not rebutted by the Applicant. *See In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992) (the burden of presenting an initial prima facie case of unpatentability is on the examiner, after which the burden of coming forward with rebuttal evidence shifts to the applicant; the ultimate burden of proof of unpatentability is with the examiner).

Panel overlooked the rebuttals Appx7716-7718; Appx7721-7724; Appx7901-7906; Appx8017-8021; Appx8031-8037; UBBr76-78; though not necessary because independent claims are INDISPUTABLY not anticipated by the references. See #14-15.

EXAMINER AND PTAB MUTILATED CLAIMS AND SPECIFICATION, AND DISREGARDED APPELLANT'S ASSERTED INTERPRETATION OF TERMS ON RECORD, PHOSITA TESTIMONY, AND RECONSTRUCTED CITED ART TO RULE ANTICIPATION. PANEL HAS AFFIRMED THE SAME. THE COURT HAS NOT FUNCTIONED AS APPEAL COURT. IT HAS RUBBER STAMPED PTAB.

II

SECTION 101

The examiner and the Board also held that all of the claims are directed to non-statutory subject matter under Section 101, because the claimed fatty acid mixtures occur naturally in walnut oil and olive oil. The examiner found that the claimed "intermixture of lipids from different sources" is "structurally indistinct" from lipid formulations derived from a single source, as shown in the prior art. The examiner also found that the claims are directed to natural products of walnut oil and olive oil, and that the additional limitations in the claims do not change the characteristics of the products, or add "significantly more" to the claims.

The Applicant argues that it "disclaimed" the claim scope of compositions from a single source, thus avoiding not only anticipation, but also Section 101. The Applicant

PANEL HAS FAILED TO REVIEW §101 DE NOVO AS PER LAW. #16.

PANEL ACKNOWLEDGES APPLICANT DISCLAIMED SINGLE SOURCE PRODUCT OF NATURE, THEN DISREGARDS THE FACT IN FURTHER ANALYSIS. #21-22.

A. "dosage" and "casings providing controlled delivery" CHANGE FUNCTIONALITY of omega-6 and omega-3, as they occur in nature, and DO add significantly more to nature. §101 INQUIRY IS OVER AT THIS POINT. "Step one" Mayo. #17.
B. Claims are drawn to an extremely important inventive concept which confers eligibility. "Step two" Mayo. #18.
C. Claims on the whole are patent eligible. #19.
D. Claims do not recite any oil. No requirement under §101 to show distinction over product not recited in claims. #20.
E. Single source oil including by-process was disclaimed. #21-22.
F. Oils are not products of nature.
G. Instructions cited from references are not products of nature. #25.

states that the Board erred in rejecting all of the claims as directed to a product of nature, arguing that the claimed "intermixture of lipids from different sources" does not occur in nature, and that the properties of the claimed formulations from different lipid sources are different from the properties of single source natural products.

Preponderance of evidence as scientific publications and four PHOSITA testimonies have been submitted that claimed mixtures have properties that do not occur in nature. #23-24.

PANEL ACKNOWLEDGES "DOSAGE" AND "CASINGS PROVIDING CONTROLLED DELIVERY" DO NOT EXIST IN NATURAL PRODUCTS AND THEN DISREGARDS THE FACT IN FURTHER ANALYSIS.#17.

The Applicant also argues that the claimed limitations of "dosage" and "casings providing controlled delivery" do not exist as natural products. The Applicant states that natural products cannot provide a controlled delivery or dosage because lipid profiles in nature are unpredictable. The Applicant also states that walnut oil and olive oil are not "natural products," for they can be obtained only by treatment of natural products.

Panel moves on to Claims 128, and others without concluding patentability of independent claims 65, 91, 129, and 130.

Claim 128

The Applicant also argues that claim 128 is distinguished from natural products, and is not anticipated based on the limitation that the compositions contain "nuts or their oils" obtained from "almonds, peanuts, and/or coconut meat." The Board held that admixture with other natural products of known composition was not shown or stated to change the nature of the compositions, citing *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 131 (1948) ("The combination of species produces no new bacteria, no change in the six species of bacteria, and no enlargement of the range of their utility. . . . They serve the ends nature originally provided and act quite independently of any effort of the patentee.").

A. Decision37 did not make the statements panel has made here. Decision alleged claim 128(1) is a product-by process claim drawn to olive/walnut oil. Appellant asserted almonds, peanuts, and/or coconut meat are compositionally different from olive/walnut oil.
B. Mixing almonds/peanuts/ coconut with omega-3/omega-6 as claimed changes the compositions. Nature did not intend almonds/peanuts/ coconut to have omega-3 amounts claimed. Each have certain antioxidants which mixed with claimed omega-6/omega-3 changes their properties and use. Panel has overlooked this from Specification. Appx60-64. #27.

The Board correctly held that claim 128 does not avoid the rejection on the ground that the claims are directed to known natural products.

Claims 102, 107, and 119

The examiner and the Board did not specifically include claims 102, 107, and 119 in the rejection for antici-

pation, as the PTO recognizes, stating that "Bhagat advances arguments regarding olives and walnuts for claims 102, 107, and 119. Bhagat Br. 77–78. The Board did not issue a rejection for these claims based on either olives or walnuts." PTO Br. 38 n.10. However, the PTO states that these claims were properly rejected under Section 101.

Claim 102 recites specific ratios of polyunsaturated, monounsaturated, and saturated fatty acids. Claims 107 and 119 present the fatty acid content recited in claims 98 and 91, respectively, in Tables in the specification. The Board observed that the servings of olive oil and walnut oil shown in the references contain omega-6 and omega-3 fatty acids in amounts within the Applicant's claimed ranges. Thus the Board held that the "intermixture of lipids from different sources" does not distinguish the claims from natural products because the Applicant "has not provided adequate evidence that an oil from different sources would necessarily have a composition that is different from one from the same source, nor that a different source would necessarily impart characteristics to the formulation which were absent when a single source was used." Board Op. at *8.

The Applicant argues that the Board erred, and that the claimed mixtures of fatty acids from different sources are "structurally different" from the single-source walnut oil and olive oil. The Applicant points to the '034 specification's statements that the claimed mixtures provide benefits of "synergy" and "avoid concentrated delivery of specific phytochemicals that may be harmful in excess," J.A. 62 ¶30. The Board held that these arguments do not overcome the identity of the claimed products and the naturally occurring lipid profiles of walnut oil and olive oil. The Board cited the references showing the lipid content of natural walnut oil and olive oil, and pointed out that the claims include this lipid content. The Board pointed out that the specification does not distinguish the

Panel has conflated analysis of independent claims with dependent Claims 102, 107, and 119. Panel starts to discuss dependent claims 102, 107, and 119 then drops the analysis...

....here and shifts to independent claims 65, 91, 129, and 130.

Appellant rebutted Decison37 to be safe. If Appellant had not, it could have been used against the Appellant.

Panel overlooked the briefs that Claim 102 recites, "ratio of monounsaturated fatty acids to polyunsaturated fatty acids is in the range of 1:1 to 3:1" and that neither olive nor walnut oil meet the limitation, and similarly elements combined in tables 7-20 in Claim 107 and 119 are outside the scope of the cited oils. Examiner failed to cite a single product, even an oil, that meets the limitations in Claim 102, 107, and 119. See #26.

A. As per law, "servings" are instructions, not product of nature. #25.
B. As per law, "intermixture" is capable of structural limitation. #5.
C. Under §101 there is no requirement to distinguish claims from products (oils) not recited in claims. #20.
D. Oils are not natural. #25.
E. Single source oil including by-process is disclaimed, i.e. the intermixture is NECESSARILY distinct v single source #21-22.
F. OVERWHELMING EVIDENCE including five scientific publications (Appx6650-6707) and four PHOSITA testimonies have been submitted that oils are not products of nature and claimed mixtures necessarily have properties not found in nature. #23-24.

claimed omega-3 and omega-6 fatty acids, from the omega-3 and omega-6 fatty acids that exist in nature, and that the Applicant has not provided evidence of such distinction.

The Applicant argues that while naturally occurring plants or their isolated lipids may be natural products, extracts and composites or mixtures are not natural products because the extraction processes required to obtain edible oils from olives and walnuts transform the claimed lipids from natural products. The Board found, and we agree, that the Applicant has not shown that the claimed mixtures are a "transformation" of the natural products, or that the claimed mixtures have properties not possessed by these products in nature.

The Board concluded that the claims are directed to the omega-6 and omega-3 fatty acids that occur in nature, and that the asserted claim limitations do not distinguish the claimed products and compositions from those shown in the cited references. We have considered all of the Applicant's arguments, and conclude that substantial evidence supports the Board's findings, and the rulings of unpatentability.

AFFIRMED

No costs.

PANEL ACKNOWLEDGES OILS ARE TRANSFORMED FROM PRODUCTS OF NATURE THEN DISREGARDS THE FACT IN FURTHER ANALYSIS AND STILL REQUIRES APPLICANT TO DISTINGUISH CLAIMS FROM CITED OILS. #25.

PANEL FAILS ITS DUTY TO DETERMINE §101 ELGIBILITY DE NOVO WITHOUT DEFERENCE AS PER LAW. #16.

PANEL FAILS TO CITE ANY LAW WHY INDEPENDENT CLAIMS ARE NOT PATENATBLE.

PANEL HAS OVERLOOKED TO REVIEW CLAIMS 68, 73, 74, 77, 78, 98, 118, 121-122, AND 124 UNDER §101. UBBr53, 58-59. #28.

Preponderance of evidence including five scientific publications (Appx6650-6707) and four PHOSITA testimonies have been subimtted that in nature omega-6/omega-3 always occur with certain phytochemicals in configurations necessarily altered by manipulations, e.g. storing, extracting, mixing, encasing... E.g., Gotoh (Appx6696) evidences even changing ratios of omega-3 and omega-6 affect each other in oxidative stability. UBBr12, 16, 53, 59; UBRBr15-16. "Applicant has not shown [evidence]…" is false. #23-24.

A. Claims are drawn to "dosage" and "casings providing controlled delivery" which CHANGE FUNCTIONALITY of omega-6 and omega-3, as they occur in nature, and DO add significantly more to nature. §101 INQUIRY IS OVER AT THIS POINT. "Step one" Mayo. #17. Claims do not recite any oil. No requirement under §101 to show distinction over product not recited in claims. #20.

B. Claims are drawn to an extremely important inventive concept which confers eligibility. "Step two" Mayo. #18. p18-23 of the petition.

C. Claims on the whole are patent eligible. #19.

ANNEX I:

Petition for Panel Rehearing and Rehearing En Banc to US Court of Appeals for the Federal Circuit of April 25, 2018

Addendums:

- Annotated Copy Of The Court's Opinion Sought To Be Reheard, **omitted** since it is attached here as Annex H
- "Federal Circuit Finds Composition of Matter Ineligible For Patenting," March 27, 2018. Opinion by Courtenay Brinckerhoff, BS chemistry; IP Partner at Foley & Lardner Chemical Practice; Admitted at CAFC.
- "In Re Urvashi Bhagat: One More Decision Denying Patent Eligibility of Nature-Based Product Claims," March 29, 2018. Opinion by Marina Miller, PhD. molecular biology/biochemistry; IP Partner at Oblon Chemical Patent Prosecution group; Admitted at CAFC.
- "In re Urvashi Bhagat – The Slippery Slope of Natural Product Claims," March 22, 2018. Opinion by Warren Woessner, PhD organic chemistry; Patent Attorney; founding shareholder of Schwegman Lundberg & Woessner; Admitted at CAFC.
- "Omega-6 fatty acid" Wikipedia, accessed March 5, 2018, **omitted** since it is attached here as Annex AC
- Patents for Humanity Application (Repeated from Joint Appendix, Appx7908-7915, for emphasis); **omitted** since it is attached here as Annex R.

2016-2525
(Serial No. 12/426,034)

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

IN RE BHAGAT

APPEAL FROM THE UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT TRIAL AND APPEAL BOARD

APPELLANT'S COMBINED PETITION FOR PANEL REHEARING AND REHEARING *EN BANC*

Pursuant to Federal Rule of Appellate Procedure 2, 35(a)(1) and (2), and 40 and Federal Circuit Rule 35 and 40, Appellant hereby petitions this Court to order a panel rehearing and rehearing *en banc* of this appeal.

Urvashi Bhagat
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Pro se Appellant

Dated: April 25, 2018

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- "In Re Urvashi Bhagat: One More Decision Denying Patent Eligibility of Nature-Based Product Claims," March 29, 2018. Opinion by Marina Miller, PhD. molecular biology/biochemistry; IP Partner at Oblon Chemical Patent Prosecution group; Admitted at CAFC.

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- "Omega-6 fatty acid" Wikipedia, accessed March 5, 2018

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TABLE OF ABBREVIATIONS

In addition to the abbreviations set forth in Appellant's Opening Brief (at vii-viii) and Reply Brief (at vi), following abbreviations are used in this petition.

BRI	Broadest Reasonable Interpretation
UBRBr____	Appellant's Reply Brief at page____
UBRBr___,… ___	Appellant's Reply Brief at page____, and page____
Opinion	Opinion, In re Bhagat, 2016-2525 (Fed. Cir. Mar. 16, 2018)
Op___	Opinion, In re Bhagat, 2016-2525 (Fed. Cir. Mar. 16, 2018) at page____
Op____,… ___	Opinion, In re Bhagat, 2016-2525 (Fed. Cir. Mar. 16, 2018) at page____, and page____
WikipediaOils	https://en.wikipedia.org/wiki/Vegetable_oil#Production
WikipediaNormann	https://en.wikipedia.org/wiki/Wilhelm_Normann
CBOp___	"Federal Circuit Finds Composition of Matter Ineligible For Patenting," March 27, 2018, at page____. Opinion by Courtenay Brinckerhoff.
MMOp___	"In Re Urvashi Bhagat: One More Decision Denying Patent Eligibility of Nature-Based Product Claims," March 29, 2018, at page____. Opinion by Marina Miller, PhD.
WWOp___	"In re Urvashi Bhagat – The Slippery Slope of Natural Product Claims," March 22, 2018, at page____. Opinion by Warren Woessner, PhD

All emphasis in this petition is added unless otherwise indicated.

STATEMENT PURSUANT TO FEDERAL CIRCUIT RULE 35(b)(2)

I. Based on my professional judgment, I believe the panel decision is contrary to the following decisions of the Supreme Court of the United States and the precedents of this court: *In re Imes,* 778 F.3d 1250, 1251, 1254 (Fed. Cir. 2015); *In re Zletz*, 893 F.2d 319, 321-22 (Fed. Cir. 1989); *TriVascular, Inc. V. Samuels,* 812 F.3d 1056, 1061-62 (Fed. Cir. 2016); *In re Cortright,* 165 F.3d 1353, 1358 (Fed. Cir. 1999); *In re Alton*, 76 F.3d 1168, 1175-77 (Fed. Cir. 1996); *In re Gulack*, 703 F.2d 1381, 1385 (Fed. Cir. 1983). *Markman v. Westview Instruments, Inc*., 52 F.3d 967, 978 (Fed. Cir. 1995)(en banc); *Phillips v. AWH Corp.* 415 F.3d 1303, 1313-1314 (Fed. Cir. 2005)(en banc); *Teva Pharms. USA Inc. v. Sandoz Inc.,* 135 S.Ct. 831, 837 (2015); *Perricone v. Medicis Pharmaceutical Corp*, 432 F.3d 1368, 1375-79 (Fed. Cir. 2005); *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993); *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988); *In re Elsner,* 381 F.3d 1125, 1127 (Fed. Cir. 2004); *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.,* 851 F.3d 1270, 1274 (Fed. Cir. 2017); *In re Robertson,* 169 F.3d 743, 745 (Fed. Cir. 1999); *Lindemann Maschinenfabrik GMBH v. Am. Hoist & Derrick Co.*, 730 F.2d 1452, 1458-59 (Fed. Cir. 1984); *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1371 (Fed. Cir. 2008); *In re Bilski*, 545 F.3d 943, 951 (Fed. Cir. 2008) (en banc); *Rapid Litigation Management Ltd. v. Cellzdirect*, 827 F. 3d 1042, 1047-50 (Fed. Cir. 2016); *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S.

Ct. 1289, 1296-97 (2012); *Alice Corp. v. CLS Bank International*, 134 S. Ct. 2347, 2355 (2014); *Classen Immunotherapies, Inc. v. Biogen Idec,* 659 F.3d 1057, 1063-68 (Fed. Cir. 2011); *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.* 133 S. Ct. 2107, 2119 (2013); *In Re Hans Oetiker*, 977 F.2d 1443, 1449 (Fed. Cir. 1992); *In re Garnero*, 412 F.2d 276, 278-79 (C.C.P.A. 1969); *Abbott Labs v. Sandoz,* 566 F.3d 1282, 1294 (Fed. Cir. 2009)(en banc); *Funk Bros. Seed Co. v. Kalo Inoculant Co.,* 333 U.S. 127, 131, 135 (1948); *Diamond v. Chakrabarty, 447 U.S. 303, 309-10 (1980); In re Miller*, 418 F.2d 1392, 1396 (C.C.P.A. 1969); *Diamond v. Diehr*, 450 US 175, 188-9 (1981). Full court needs to reconsider why panel has issued an Opinion contrary to SCOTUS and this Court's numerous controlling precedents.

II. Based on my professional judgment, I believe this appeal requires an answer to one or more precedent-setting questions of exceptional importance.

A. Is it proper to disregard structural limitation "intermixture" under § 101?

B. Is it proper to require applicants to distinguish claimed products from products proven not to be products of nature under § 101?

C. Is it proper to hold functional printed matter or instructions combined with alleged product of nature as product of nature under § 101?

D. Is it proper to compromise innovation in nutrition and public health massively in favor of narrow patents, creating unfavorable economics for significant advancement in nutrition, preserving perpetual status quo?

POINTS OF LAW OR FACT OVERLOOKED OR MISAPPREHENDED BY THE PANEL

1. Contrary to *Imes* 1251, panel failed to review all claim construction ***de novo***. "Nothing in this case implicates the deference to fact findings." *Imes*. UBBr39-40.

2. Contrary to *Zletz* 321-22, panel failed to construct "dosage" in plain words of the claims (Op5), and per Applicant's interpretation of the term in prosecution.

> "determination of amount to be administered and/or administration in prescribed amounts," "controlled/specified amount to ingest at one time or regularly during a period of time." (Appx5822-5823, Appx7050, Appx7858)

"Dosage" is limiting in Specification is an **INDISPUTABLE FACT**: Four tables (9-12) titled, "Lipid Dosages…" recite specific doses; ¶34, ¶36, ¶39, ¶47-49, ¶57, ¶59, ¶67, ¶89, ¶97, ¶103 refer to "dose/dosage" as specified amount for ingestion; ¶39 and examples 11-27 teach importance of dosage and dose effect in detail; ¶39 recites, "steady **dosage** within the optimal range"; ¶67 recites, "In addition to **amount**... relatively steady **dosages**"; and ¶103 recites, "omega-6 and omega-3 are anti-inflammatory in small **doses** and inflammatory in large **doses**." PTOBr25-26, 34 concede "any orally acceptable form" refers to foods e.g., "a nutritional bar", **not** amount. Specification, e.g., at ¶36, ¶68, and Appx2966 teach to combine foods to achieve specific "dosage" of fatty acids. UBBr41-44; UBRBr2-3, 28-29. To allege "dosage" is not limiting in view of above is simply **NOT** reasonable.

3. Contrary to *Imes* 1254 and *TriVascular* 1061-1062, panel overlooked (Op5) the plain meaning of the claims in context of surrounding words. E.g., independent

claims recite, "casings providing controlled delivery of the formulation to a subject," not just "casing" (Op5); and Claim 65 recites, "A lipid-containing formulation, comprising a dosage of omega-6 (main clause)…wherein …omega-6 fatty acids are not more than 40 grams (subordinate clause)." The panel improperly divorced main clause from the subordinate clause (Op8). Contrary to *Zletz* 321-22, panel overlooked Applicant's prosecution interpretation. UBBr28-30, 41, 44-45.

> "Casings…designed to contain one or more dosages of the formulation in order to control the delivery (e.g., substantially avoid inadequate or excess delivery and/or substantially control release.)" Appx7048, Appx7301-7302.

4. Contrary to *Cortright* 1358, panel overlooked BRI must be consistent with PHOSITA interpretation; panel's interpretation of "dosage" and "casings providing controlled delivery of the formulation to a subject" (Op5) conflicts with PHOSITA testimony and meaning given to "dosage" in analogous patents. UBBr41-42, 44-45.

> "The use of the word 'dosage' in the subject patent application is clearly directed to determination of amount to be administered and/or administration in prescribed amounts (see para 34, 39, 47, 48, 49, 57, 59, 89, 97, 101, and 103)." (Appx6485 ¶12, Appx6502 ¶12, Appx6519 ¶12)
>
> "As part of the correct fatty acid delivery teaching the following is clearly evident from the specifications…c. Omega-6 dosage less than 40 grams (Tables 9, 10, 11, 12, 13)." (Appx6488 ¶17c, Appx6505 ¶17c, Appx6522 ¶17c.)
>
> "In light of the specification of the subject patent application, 'casing' or 'one or more complementing casings providing controlled delivery of the formulation' in amended claims 65, 91, 129 and 130 means one or more casings that are designed to contain one or more dosages of the formulation in order to control the delivery (e.g., substantially avoid inadequate or excess delivery and/or substantially control the release). This is clear from, for

example, paragraphs 10, 34, 37, 60, 61, and Tables 16-19 of the specification." (Appx7230 ¶5, Appx7239 ¶, Appx7320 ¶5)

5. Contrary to *Garnero* 278-79, *Abbott* 1294, panel disregarded "intermixture of lipids from different sources" as a structural limitation, and disregarded that the structure of claimed products is not fully known, too complex to analyze, and expected to have unnatural properties (#23-24 infra). UBBr52-53; UBRBr4-7.

6. Contrary to *Alton* 1177, panel inexplicably overlooked eleven PHOSITA testimonies. Appx3849-3869; Appx5702-5705; Appx6479-6529; Appx7228-7245; Appx7318-7327; Appx7356. UBBr43-45, 62, 65-66, 70, 75; UBRBr15, 21-22, 24.

7. Contrary to *Gulack* 1385, panel excised "providing controlled delivery of the formulation to a subject" (Op5-8) and "intermixture of lipids from different sources" (Op6-8), and mutilated "a dosage of omega-6…wherein …omega-6 fatty acids are not more than 40 grams" from claims (Op5, Op8); "dosage" and "casings providing...subject" are acknowledged at Op10, but excised in analysis at Op10-12.

8. Contrary to *Gulack, TriVascular,* and *Cortright,* panel overlooked in-context interpretation of all claims consistent with PHOSITA interpretation. UBBr41-49.

9. Contrary to *Markman* 978, *Phillips* 1313-1314, and *Teva* 837, panel failed to determine "ordinary meaning" and "scope" of Mark ***de novo*** as a matter of law in **temporal context**. There is no implication of deference to fact finding here. Panel failed to read Mark's "lipid" means lipid source that include non-lipids (col.5.ll.59-62) and "source" means source of nutrients (col.4.ll.19-20). Mark discloses

"omega-**3** to omega-**6** fatty acid ratio of approximately 4:1 to 6:1" in col.2.ll.37-38, **not** "omega-6 to omega-3 fatty acid ratio of approximately 4:1 to 6:1" (Op3); and "the **source** of omega-6 fatty acids is present in a range of approximately 4-6% of the total calories. The omega-3 fatty acid **source** is preferably present in the range of approximately 0.8-1.2% of the total calories" (col.4.ll.27-31), **not** "omega-6 [omega-3] fatty acid is present in a range of…" Op3-4. UBBr30-33, 60, 62-65. Contrary to *Perricone* 1376-79, panel assumed something Mark did **NOT** disclose and overlooked Mark does not necessarily function as claimed.

10. Contrary to *Perricone* 1376-79 and *Elsner* 1127, panel overlooked Mark **does not enable** "dosage **of** omega-6 and omega-3" with any example, which is different among children 1-10 years old (O6 1-10g for infants; Appx71-72) as PHOSITA testified (Appx7324-7325). Op4 admits "Mark's daily dosage **may** include 1,000 mL, as the table in column 4 refers to g/1,000 mL," but to anticipate Mark must **necessarily, not may**, function as "dosage", which it doesn't, stating no toxicity even at 2500 kcal/day (O6 16.7g for infants) (col.5.ll.10-12). UBBr60-62. Contrary to *Alton* 1177, panel overlooked PHOSITA testimony. UBRBr21-22.

11. Contrary to *Nidec* 1274, *Robertson* 745, *Lindemann* 1458-59, and *Net Money* 1369-71, panel overlooked Mark does not disclose the part-to-part relationship "arranged as in the claim". UBBr17-18, 23-26, 66-67. In *Nidec* 1274, Judge Taranto of this panel ruled "*Kennametal* does not permit the Board [or this

panel] to fill in missing limitations simply because a skilled artisan would immediately envision them." Mark recites conflicting ratios scattered over the disclosure, incomplete lipid profiles in inoperable tables in columns 4 and 6, does not necessarily function as "dosage" or "intermixture." Contrary to *Gulack* 1385, panel mutilated claims, contrary to *Rijckaert* 1534 and *Fine* 1075 panel optimized Mark, and contrary to *Oetiker* 1445 panel overlooked preponderance of evidence *Mark* discloses incomplete data to rule anticipation. UBBr62-66; UBRBr17-26.

12. The panel overlooked to review several claims under Mark, e.g., independent Claims 129 and 130, and dependent claims 68, 69, 73, 96, 98, 100, 142, and 144. Op4 misapprehends, Claim 82 (dependent on 65) and independent Claim 91 are not rejected under Mark by PTO. Decision38. UBBr67-68; UBRBr26.

13. Contrary to *Zletz* 321-322, despite acknowledging "prosecution disclaimer of…olives and walnuts" (Op7), panel overlooked this **UNDISPUTED FACT** in ruling anticipation by WebOlives/WebWalnuts (Op7-9). UBBr69-71.

14. Contrary to *Nidec* 1274, *Robertson* 745, *Lindemann* 1458-59, and *Net Money* 1369-71, panel overlooked WebOlives/WebWalnuts do not disclose the part-to-part relationship "arranged as in the claim." WebOlives/WebWalnuts are **INDISPUTABLY not anticipatory**; **neither discloses "an intermixture of lipids from different sources," let alone "dosage"/"casings...subject."** Contrary to *Alton* 1175-1177, panel overlooked PHOSITA testimony holds the references do

not teach "dosage" of omega-6/omega-3, stating, "The concentration of nutrients per cup of olives in the reference fails to disclose such predetermined/ prescribed amount to quantify the olives for a person to eat." Anticipation law "does not permit the Board [or this panel] to fill in missing limitations," *Nidec* 1274, which PHOSITA do not even envision. Appx6484-6485; Appx6501-6502; Appx6518-6519; Appx7234-7235; Appx7243-7244; Appx7325-7327. The references do not necessarily function as dosage at omega-6 to omega-3 >4:1; they teach random consumption of food mixtures (Appx6966-6967, Appx6981), wherein overall ratio of omega-6 to omega-3 is around 2:1 (Appx6142). UBBr68-76; UBRBr27-31.

15. Panel overlooked rebuttal to alleged anticipation of dependent claims (Op9) by WebOlives/WebWalnuts; Appx7716-7718; Appx7721-7724; Appx7901-7906; Appx8017-8021; Appx8031-8037; UBBr76-78; though not needed (#14 supra).

16. Contrary to *Bilski* 951 and *Rapid* 1047, the panel overlooked to review § 101 patent eligibility ***de novo***, as a question of law **without deference**. UBBr40.

17. Contrary to controlling SCOTUS rulings *Mayo* 1296-97 and *Alice* 2355, and *Rapid* 1047, the panel overlooked **§ 101 inquiry is over at "step one"**; despite acknowledging (Op10) the features "dosage" and "casings providing controlled delivery" change functionality of omega-6 and omega-3, as they occur in nature, panel overlooked the features in eligibility analysis at Op10-12 and that they do add "significantly more" to natural products. UBBr51-53; UBRBr3-4, 12-14.

18. Contrary to controlling SCOTUS rulings *Mayo* 1296-97 and *Alice* 2355, and *Rapid* 1050, **"step two"** of § 101 inquiry (though not needed; #17 supra), the panel overlooked **extremely important inventive concept** is present in the claims as a whole and vast immediate and downstream public health benefit is expected from the solutions because the claimed subject matter is critical for health yet poorly understood. Prior art overwhelmingly teaches omega-6 to omega-3 ratio <4:1, omega-6 <10% of total fat and <6.67g/day, and teaches suppression of omega-6, which is deleterious; lipids are unpredictable in natural sources; 99% of public does not know the ABCs of lipids; due to all this public health suffers at large scale; 117 million people live with associated diseases; ~million die/year; and ~$3 trillion/year is spent on the related diseases. UBBr3-10, 54, 79-81; UBRBr1-4.

19. Contrary to *Diehr* 188-9, *Rapid* 1048, and *Classen* 1068, panel has failed to consider **claims on the whole are patent eligible.** Claimed combination of "formulations", "dosage of omega-6 and omega-3", "casings providing controlled delivery of the formulation to a subject", "intermixture of lipids from different sources", and the extremely important inventive concept is sufficient to confer eligibility. No further analysis/evidence is needed. UBBr3-9, 36, 54; UBRBr12-16.

20. Contrary to controlling SCOTUS ruling *Mayo* 1295-97, and this Court in *Classen* 1063-68 and *Rapid* 1047-50, each holding **§101 separate from §§102 and 103** that if plain language of the claims is not directed to patent ineligible concept,

§101 inquiry is over and the claims pass §101 threshold, the panel affirmed §102-type analysis in §101 eligibility (Op10-12) though Claims 65, 91, 129, and 130 do not recite the cited oils. Dependent claims 142-143 (Appx7743-7744) illuminate claimed "intermixture" can be free fatty acids or other forms pointing to distinctions over a single source. UBBr36, 45-46. Thus, claimed products can simply be "dosage" of omega-6 and omega-3 in "casings providing controlled delivery of the formulation to a subject," whereas oils contain 100s of components. **Overwhelming evidence is on record minor lipid manipulations confer marked changes on starting product and changes in omega-6/omega-3 ratios affect their properties**. UBBr53; #23-24 infra. The panel improperly held the claims indistinct from oils, not recited in claims. UBBr54-56; UBRBr7-10.

21. Contrary to *Zletz* 321-22, despite acknowledging prosecution disclaimer to "single source" at Op9, panel overlooked it in eligibility analysis. Op10-12.

22. Contrary to controlling SCOTUS ruling *Myriad* 2119, panel overlooked a variety of oil "by process" was also disclaimed. Thus, by definition claimed product is necessarily distinct from "single source". UBBr36, 45-46. UBRBr8.

23. Contrary to *Alton* 1177, panel overlooked PHOSITA testimonies that claimed mixtures have properties not found in nature. UBBr45-46. UBRBr15-16.

> "The only way to obtain [claimed mixtures] comprising omega-6 and/or omega-3 fatty acids is to either mix plant/animal tissue itself or extract omega-6 and/or omega-3 fatty acids in free fatty acid form and then mix them. Either way the physical and chemical properties of the resulting

> mixture will be significantly and markedly different from what occurs in nature because composition of triacylgycerols versus free fatty acids will change, and composition of prooxidants versus antioxidants will change [citing *Chaiyasit* et al. Appx6650-6668, and *Chen* et al. Appx6669-6685]."
>
> "Lipid sources, such as oils, butters, nuts, seeds, and herbs have 100s of compounds. Therefore, when lipids from different sources are intermixed, the resulting mixture will necessarily have different physical and chemical properties, as discussed above. A hypothetical mixture of lipids from Source A and lipids from Source B, where the resulting mixture has exactly the same properties as Source A or B is first practically impossible, and second, if possible, it would be an extremely complex scientific endeavor. There would be no motivation for a skilled artisan to intermix lipids from Source A and Source B to achieve exactly the same properties as Source A or Source B in the resulting formulation."
> Appx6493-6494¶24; Appx7230-7231¶7-8; Appx7239-7241¶7-8; Appx7320-7321¶6-8.

24. Contrary to *Oetiker* 1449, panel overlooked **preponderance of evidence** including five scientific publications (Appx6650-6707) and four PHOSITA testimonies (#23 supra) that in nature omega-6/omega-3 always occur with certain phytochemicals in configurations necessarily altered by manipulations, e.g. storing, extracting, mixing, encasing... E.g., *Gotoh* (Appx6696) evidences even changing ratios of omega-3 and omega-6 affect each other in oxidative stability. UBBr12, 16, 53, 59; UBRBr15-16. Op11-12 "Applicant has not shown [evidence]…" is false.

25. Contrary to SCOTUS ruling *Myriad* 2119 and *Chakrabarty* 309-10, despite accepting at Op10 walnut/olive oil are not "natural products" panel overlooked it in analysis at Op10-12, still comparing claims to WebOOil/WebWOil, which are A) disclaimed, B) not natural products as oils, and C) patented with unnatural cited

instructions present in the claims. *Gulack* 1385; *Miller* 1396. Op12 "limitations do not distinguish the claimed products and compositions from those shown in the cited references," overlooks references are NOT natural. UBBr54-57.

26. Contrary to *Myriad* 2119, panel overlooked Claims 102, 107, and 109 composition is structurally distinct from products of nature **on the face**.

> "Examiner has admitted '*Relative to the compositions of Claims 102, 107, and 119, there does not appear to be a naturally occurring counterpart to all of these elements present together in the claimed combination"* (Appx7776)…Claim 102 recites, "ratio of monounsaturated fatty acids to polyunsaturated fatty acids is in the range of 1:1 to 3:1" [] neither WebWOil (mono:poly 1:2.8) (Appx6985) nor WebOOil (mono:poly 7:1) (Appx6970) meet the limitation, and similarly tables 7-20 in Claim 107 and 119 [mono:poly 1:1.7-5:1] are outside the scope of WebWOil/WebOOil (Appx7961-7962). UBBr34; 58-59.

27. Contrary to *Myriad* 2119, panel overlooked Claim 128(1) composition is structurally distinct from natural products **on the face**, and mixing almonds/ peanuts/coconut with claimed omega-6/omega-3 ranges alters use. Appx60-64.

> The Examiner has not met his burden of proof to provide evidence that a almonds, peanuts, and/or coconut meat meet the limitations "…wherein… omega-3 fatty acids are present at 0.1% to 30% by weight." Table 2 of Appellant's specification and Scientific Psychic [Appx6054-6055] evidence that at least some varieties of almonds, peanuts, and coconuts, and their oils, have no omega-3 content at all, and that their omega-6 concentration is at most 32%..."Walnut Oil" evidences that its concentration of omega-3 is over 13% and omega-6 is over 58%..."Olive Oil" evidences that its concentration of omega-3 is over 0.7%. Appx7694; Appx7879-7880. UBBr16-17, 49, 59.

28. Panel failed to review many dependent claims under § 101. UBBr53, 58-59.

29. Additional oversights are annotated on the copy of Opinion in Addendum.

ARGUMENTS IN SUPPORT OF REHEARING

The Opinion is contrary to large body of law and overlooks most of Appellant's arguments (UBBr 81 pages and UBRBr 41 pages) and evidence (1421 pages of appendix showing opposite teachings including in alleged anticipatory references and 10 written (Appx3849-3869; Appx5702-5705; Appx6479-6529; Appx7228-7245; Appx7318-7327) and one oral (Appx7356-7357) PHOSITA testimony) that combination of claimed elements "dosage of omega-6 and omega-3", "casings providing controlled delivery", and "intermixtures" in defined "ratios" are not natural, are not disclosed in prior art, are not obvious, and represent an extremely important invention. The panel overlooked at least the 28 points cited supra. For example, Op4 admits Mark may, but not necessarily, functions as "dosage," but contrary to *Perricone* 1376 disregards this in ruling anticipation. Op7 admits Appellant disclaimed compositions "from single source", but then fails to explain at Op8-9 why undisputed "intermixtures of lipids from different sources" are anticipated by WebOlives/WebWalnuts. Further, Op10 admits, "the claimed limitations of 'dosage' and 'casings providing controlled delivery' 'do not exist as natural products" but then fails to explain why claimed products including the features are unpatentable at Op10-12. The Opinion renders a decision without explanation, violating Court's Operating Procedure #10(3). *Herrmann* 600 and *Soni* 751, hold failure to answer an argument is tantamount to conceding there is

no answer. Several esteemed patent attorneys and PHOSITA, unaffiliated with Appellant, also find the Opinion to be deficient, see below and addendum for detail.

> "For the most part, the court states that each PTAB finding was "correct" without explanation... The Federal Circuit acknowledged the Applicant's arguments that 'casings providing controlled delivery' 'do not exist as natural products,' but did not address those arguments in its § 101 analysis." CBOp2.
>
> "The Applicant offered a number of arguments for patent eligibility but the court agreed with the Board...the analysis under section 102 was [] applied to the analysis under Section 101. However, as explained by the Supreme Court in Mayo, the analysis under section 101 is separate from the patentability analysis under sections 102 or 103. Here, the main claim appears to include limitations that are not nature-based or that add "significantly more" to the nature-based product, e.g., the limitations 'dosage' and 'casings providing controlled delivery' are not found in nature and natural counterpart products and the claimed mixture 'avoids concentrated delivery of specific phytochemicals that may be harmful in excess." MMOp1-2.
>
> "In fact, the main claim used as representative do contain limitations that are not nature-based products, and impart at least functional structure to the claims. The claims require that the composition comprised a dosage of the fatty acids, contained in 'one or more complementing casings providing controlled delivery of the formulation to a subject...' Applicant's controlled release dosage form does not exist in nature and changes the characteristics of the acids as they occur in their natural state, in walnuts or olives...the need to distinguish the products from the prior art is not even a requirement... Applicant deserved better than the courts use of the 'naked' anticipation rejection to meet the standards for a judicial exception under s.101." WWOp2-3.

Thus, patent attorneys and PHOSITA, unassociated with Appellant, agree,

A. the panel regurgitated and rubber-stamped PTO improprieties;

B. the panel's holdings are contrary to SCOTUS and this Court's precedents;

C. "dosage" and "casings providing controlled delivery" are limiting and that they "impart at least functional structure to the claims"; and

D. the panel disregarded Appellant's submissions and Appellant deserved better than the panel's treatment.

Appellant submitted an intense appeal, with evidence of mass confusion, opposite teachings including from cited art, and large-scale public suffering (~117 million people) and national cost (~$2.6 trillion/year). UBBr3-10, 54, 79-81; UBRBr1-4. **In reply, the panel issued an opinion overturning a large body of binding law, even SCOTUS, labeled "non-precedential!" It is illogical.** Appellant pleaded PTO abused the Appellant and millions of Americans who might have benefited from the solutions (UBBr8-9, 38, 77, 80-81; UBRBr1-4); now the panel has abused the Appellant (and the millions of Americans), **applying more stringent—contrary to law and disregarding arguments and evidence—rather than less stringent standards applied to *pro se*.** *Haines* 520; *Baldwin* 164.

The disjointed evasive Opinion is uncharacteristic and unexpected of this esteemed panel (known to take positions as taken by Appellant, Judge Newman authoring *Zletz*, dissenting *Abbott*; Judge Taranto ruling *Nidec*; Judge O'Malley authoring *TriVascluar*), and the 2nd highest seat of justice in United States of America the "most advanced country." If such opinions can be issued at this level then inventors can have no confidence in justice. The case should be reheard.

ARGUMENTS IN SUPPORT OF REHEARING EN BANC

I. Opinion Conflicts With Binding Precedents from SCOTUS and this Court

The Opinion conflicts with binding precedents from SCOTUS and this Court cited supra and in UBBr and UBRBr. The opinion in principle invalidates 1000s of patents drawn to "new and useful…composition of matter" as per 35 USC §101, for example, US7759507B2, US8282977B2, and US9034389B2. The panel circumvents this by being evasive and issuing "non-precedential" opinion, but A) the Appellant will petition the Opinion be made precedential because it attempts to alter the existing rules of law, establishing new rule of law, creating conflict within this Court's and with SCOTUS precedents (IOP#10(4)), and B) the non-precedential Opinion will be cited by parties in litigation. Indeed several attorneys practicing at this Court find the Opinion to be improper (CBOp, MMOp, WWOp). Court's docket will soon be burdened with more appeals on same issues, as litigants will be less likely to settle before an appeal when both can cite cases in their favor. Opinion evades adjudication and is confusing. For example, OP9-10 without adjudicating independent claims 65, 91, 129, and 130, drawn to "dosages" and "casings providing controlled delivery of the formulation" that do not occur in nature, moves on to claims 128, 102, 107, and 119, which were also not adjudicated (#26-27 supra). Parties are more likely to engage in lawsuits when law is unclear. The Opinion compromises judicial efficiency and fairness of the process.

II. This Appeal Requires Answers To Precedent-Setting Questions Of Exceptional Importance

A. Is it proper to disregard structural limitation "intermixture" under § 101?

The term "intermixture" is capable of construction as a structural limitation. *Garnero* 279. Further, product claims comprising such terms are patentable when structure of claimed products is not fully known, too complex to analyze, and expected to have distinct properties (#23-24 supra). *Abbott* 1294. Mutatis mutandis this law applies under § 101.

B. Is it proper to require applicants to distinguish claimed products from products proven not to be products of nature under §101?

Appellant has submitted indisputable evidence that walnut/olive oils cited under §101 are not products of nature per SCOTUS rulings. UBBr54-56; UBRBr12.

> "Oil[s] are man-made from products of nature, like walnuts or olives, through **non-natural manufacture, transforming** walnuts/olives into oils and pulp/nut flours, after which the products acquire **different names** (oil/pulp/nut flour), **character** (physical and chemical properties), and **use** (cannot germinate and nutritive worth is different), therefore are patent-eligible. *Funk; Chakrabarty; Myriad*." UBBr55. "Even the amount/concentrations of omega-6 and omega-3 are not the same in walnut/olive oil as compared to walnuts/olives." UBRBr12.

Then, is it proper to hold, "limitations do not distinguish the claimed products and compositions from those shown in the cited references [oils]" under 101? Op12.

C. Is it proper to hold functional printed matter or instructions combined with alleged product of nature as natural product under §101?

This Court has repeatedly ruled a claim directed to a combination of printed matter having a functional relationship to the subject is patentable subject matter

and is properly evaluated under §§102 and 103. *Miller* 1396, *Gulack* 1385. Mutatis mutandis, cited reference providing printed instructions—"serving" of WebOOil/WebWOil—teaches "serving" having a functional relationship to the oil, which in combination with the oil (even if oils were held to be a product of nature) is patentable subject matter. Therefore, the combination cited from WebOOil/ WebWOil is not product of nature (which in fact are patented products, U.S. Patent 7,620,531). UBBr56. Then, is it proper to hold "claim limitations do not distinguish the claimed products and compositions from those shown in the cited references [citing combination of oils with instructions] under 101?" Op12.

D. Is it proper to compromise innovation in nutrition and public health massively in favor of narrow patents, creating unfavorable economics for significant advancement in nutrition, preserving perpetual status quo?

This dispute arose because PTO compromised instant innovation holding narrow mixtures of certain oils/nuts/seeds (Claim 128(2)-(7); Appx7790) allowable but not "dosages of omega-6 and omega-3," "casings providing controlled delivery" and "intermixture of lipids from different sources" in defined ratios. Appellant declined because such practice, A) has already caused great harm to public health; B) is stalling meaningful advancement in nutrition; and C) is unlikely to generate investor interest in backing this innovation, which requires extensive public teaching therefore is a risky investment. The panel improperly affirmed PTAB using the same tactics, excising terms and context from claims and mutilating

claims, mutilating the disclosure, and disregarding prosecution avowals/disavowals, PHOSITA testimony, scientific publications on record, the extremely important inventive concept, Appellant's briefs, and this Court's and SCOTUS precedents.

Claimed inventions solve a critical long-felt unsolved problem of correct lipid delivery benefitting vast number of Americans, particularly the impoverished (Appx7911-7913). Most chronic diseases are associated with mismanaged lipid intake; and lipid intake affects immunity and daily well-being. Dosages of omega-6, omega-3, other fatty acids, lipid vitamins, and lipid phytochemicals are critical for health, where too much or too little both have serious health consequences, and lipid intake has to be relative to other lipids because lipids can materially affect the activity of each other. Yet, there continues to be mass confusion in the art and teachings opposite of instant claims. In particular, prior art, including the cited art, overwhelmingly disparages omega-6, which is a critical nutrient, and teaches low intake of omega-6 relative to other lipids and suppression of omega-6 activity—teaching omega-6 to omega-3 ratio less than 4:1 or omega-6 is less than 10% of total lipids—which '034 Application teaches can be harmful. **There has never been a nutrient more poorly understood, more vehemently, publically, and widely disparaged and debated as omega-6.** UBBr3-9. Public is still misinformed, e.g., "Omega-6 fatty acid" Wikipedia, the most widely accessed publication, still fails to teach dosage of omega-6 and role of minor lipids.

The confusion is partly because the patent practice disfavors nutrition, forces narrow nutrition patents, and favors structurally altered molecules (Appx7777).

Narrow patents are less desirable in nutrition because they create confusion, e.g., by touting of nutrients out of context (marketing spins emphasizing protected compositions of oils, nuts and seeds by one party, and opposite spins on alternate compositions or isolated fatty acids from competition), and by compromising clear public education. This has already led to dangerous imbalances in nutrition (Appx7910), e.g., hype of omega-3 and olive oil. Then public views all solutions suspiciously and "snake oils" are coined. The problem precisely is that dosages of important lipids have been out of focus, but types of oils or fatty acids have been the focus. **Consequently, confusion perpetuates and nutritional problems affecting fundamental bodily structure and function are never solved.**

No meaningful advancement in nutrition and prevention can ever be expected under such patent practice. Purpose of patent is advancement, not ineffective token patents. SCOTUS and this Court have repeatedly held advancement in the art to be paramount. *Chakrabarty* 307, *Mayo* 1294*, Myriad* 2114*, Alice* 2355, *Rapid* 1050.

> "The authority of Congress is exercised in the hope that '[t]he productive effort thereby fostered will have a positive effect on society through the introduction of new products and processes of manufacture into the economy, and the emanations by way of increased employment and better lives for our citizens." *Chakrabarty* 307.

Lipid delivery fundamental to health has not materially advanced since the

invention of food oils ~6000 years ago (WikipediaOils). Periodically, certain fatty acids or oils or low-fat teachings have been hailed, only to reverse a few years later (Appx2771-2774; Appx4733-4739). To date random oils are randomly added to foods, evidenced by WebOOil/WebWOil listing ~12 of 100s of potent components in **batch** of oils (Appx6650-6707; #23 supra) **without** guidance on potent minor lipids components, **without** guidance that nutrient concentrations may be significantly **different** in other batches of the oils (UBBr51-52), and **without** guidance on daily dosage of omega-6 and omega-3. Oil making has advanced but delivery of oil for ingestion by subjects is still archaic because incentives are misaligned. Without proper patent protection, economics are unfavorable for significant innovation in the art. It is extremely expensive to teach public and implement the solutions because of confusion and noise. Therefore, investors shy away from risking capital in the absence of significant patent protection and term.

Patent system is asking for too much from public. Public has been paying for lipid patents for at least 100 years since hydrogenated fats patent of 1902 (WikipediaNormann), but the problem of healthy lipids for public is still not solved. Rather structurally altered molecules (hydrogenated fats) favored by patent practice (Appx7777) caused public suffering for ~100 years (Appx7913). Such molecules are likely to cause more public health havoc, because no matter what new molecules are designed, public still has to depend on food for nutrition, which

create the foundation of health or disease.

Therefore, in nutrition neither piecemeal patents nor structurally altered molecules should be favored. UBBr79-80.

> Appellant's claims significantly improve over the prior art/products of nature [even oils] by limiting excess/inadequate lipids, by providing specified amounts and ratios of omega-6 and omega-3 for ingestion that were not known in the prior art, by controlling omega-6/omega-3 ratio relative to total lipids, and by controlling delivery of the formulation to a subject using casings. UBBr50-54, 79-80. As a whole, Appellant's claims correct an 80-plus year old misapplication of lipid consumption for animal/human health. UBRBr13.

It is too complex for public to formulate lipids due to the confusing teachings, unpredictability of lipids in natural sources, and that 99% Americans cannot even name lipids (Appx7910). Further, lipid requirements differ for members of the family (by body size, hormones…) adding to the complexity. 117 million Americans live with chronic diseases costing ~$2.6 trillion in annual health care. During the **nine** years the '034 Application has been pending**, 13.6 million (1.5 million in ~2 years the application has been pending at this Court) Americans have died of associated diseases** (http://www.cdc.gov/nchs/fastats/deaths.htm). Some of those lives could have been saved by the inventive solutions. UBBr8-9.

The panel has disregarded evidence in Specification, Joint Appendix, and PHOSITA testimony that the patent practice is subjecting public to unwarranted treatments causing suffering (UBBr8-9). Specification provides ~20 examples (Appx82-97), where medical system subjected (or would subject) the individual to

drugs, devices, expensive treatments, and pain and suffering, even though a large part of the suffering could have been abated by correcting the lipid delivery. If treatments are favored and made more financially rewarding by the patent practice, **then such patent practice is organized crime against humanity, then we should expect continuation in escalating healthcare costs and public suffering**.

Claimed inventions solve an 80-year old known long-felt critical unsolved problem (UBBr9), albeit the issues involve fundamental biochemistry so the problem has existed for 1000s of years. The innovation would also set humanity on a course for long-term solution to several downstream problems (Appx7914). Not granting appealed claims is tantamount to taking the position public should be kept confused, ill, and on drugs, and this 1000s of years old problem should continue into perpetuity. Ultimate purpose of research is to enhance human condition. If the solutions devised cannot be fully applied for public benefit then the patent policy is obstructing the very purpose of research. The Opinion is contrary to Congress' choice of expansive terms "composition of matter" in § 101 to "be given wide scope" and "ingenuity should receive a liberal encouragement." *Chakrabarty* 308.

CONCLUSION

Therefore, this Court sitting *en banc* should rehear this case.

Urvashi Bhagat, Pro se Appellant

ADDENDUM

NOTE: The highlights and the text in side bar have been added by the Applicant.

FOLEY

FOLEY & LARDNER LLP

Federal Circuit Finds Composition of Matter Ineligible For Patenting

By Courtenay C. Brinckerhoff and Oyvind Dahle
27 March 2018

PharmaPatents

In a non-precedential decision issued in *In re Bhagat*, the Federal Circuit affirmed the decision of the USPTO Patent Trial and Appeal Board (PTAB) that claims directed to certain lipid compositions were ineligible for patenting under 35 USC § 101. Did the court do more or less harm by rendering its decision without much explanation?

The Claims At Issue

The claims at issue were pending in U.S. Patent Application No. 12/426,034. Claim 65 was the broadest claim considered by the court:

> 65. A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater, ***contained in one or more complementing casings providing controlled delivery*** of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids from different sources, and wherein
> (1) omega-6 fatty acids are 4–75% by weight of total lipids and omega-3 fatty acids are 0.1–30% by weight of total lipids; or
> (2) omega-6 fatty acids are not more than 40 grams.

The examiner found that walnut oil and olive oil contain omega-6 and omega-3 oils in amounts within the claimed ranges, and rejected the claims under the "product of nature" paradigm based on the conclusion that the claimed formulations are not markedly different from naturally occurring walnut oil or olive oil.

The examiner also rejected the claims as being anticipated by U.S. Patent No. 5,549,905 (directed to a nutritional composition that includes omega-6 and omega-3 fatty acids) and publications of nutritional analyses of olives and walnuts showing that those natural products include omega-6 and omega-3 fatty acids in the ratios and amounts claimed.

The reference is not operable due a number of reasons, and considering temporal context, it cannot anticipate. Petition #9-12.

The PTAB upheld all rejections.

The Federal Circuit Decision

The Federal Circuit decision was authored by Judge Newman and joined by Judge O'Malley

and Taranto.

The decision summarizes the basis of the examiner's rejections, the reasoning behind the PTAB's affirmance, and the Applicant's arguments on appeal. For the most part, the court states that each PTAB finding was "correct" without explanation.

The Applicant argued that the claim language reciting an "intermixture of lipids from different sources" made the formulation markedly different from naturally occurring products, and that the formulation provided synergistic benefits and avoided "concentrated delivery of specific phytochemicals that may be harmful in excess." The Board had held that there was no evidence of record that could support that a mixture of oils from different sources is different from oil from one source. The Federal Circuit agreed, stating:

> The Board found, and we agree, that the Applicant has not shown that the claimed mixtures are a "transformation" of the natural products, or that the claimed mixtures have properties not possessed by these products in nature.

Overwhelming evidence including five scientific publications (Appx6650-6707) and four PHOSITA testimonies have been submitted that in nature omega-6/omega-3 always occur with certain phytochemicals in configurations necessarily altered by manipulations, e.g. storing, extracting, mixing, encasing... E.g., Gotoh (Appx6696) evidences even changing ratios of omega-3 and omega-6 affect each other in oxidative stability. UBBr12, 16, 53, 59; UBRBr15-16. Op11-12 "Applicant has not shown [evidence]…" is false. Petition #23-24.

The Federal Circuit acknowledged the Applicant's arguments that "casings providing controlled delivery" "do not exist as natural products," but did not address those arguments in its § 101 analysis. It did address similar arguments in its anticipation analysis, agreeing with the PTAB that the terms "casing" and "dosage" do not impart patentability, finding:

Specification does NOT say these elements are not limiting. Petition #2-4. This is a falsity, promoted by PTO upheld by Federal Circuit. It is extremely distressing that Federa Circuit would do that.

> [T]he specification states that these claim elements are not limiting, and does not describe any assertedly novel characteristics of these components or their formulations.

Thus, the court affirmed all rejections.

The USPTO Subject Matter Eligibility Examples

Could Bhagat have invoked Example 28 of the USPTO's Subject Matter Eligibility Examples? That example relates to a vaccine based on a naturally occurring peptide. According to the example, a claim reciting "A vaccine comprising: Peptide F; and a pharmaceutically acceptable carrier" does not satisfy § 101 because the carrier could be water, another natural product. On the other hand, a claim reciting "A vaccine comprising: Peptide F; and a pharmaceutically acceptable carrier selected from the group consisting of a cream, emulsion, gel, liposome, nanoparticle, or ointment" does satisfy § 101 because the recited carriers change the physical characteristics of the mixture.

The '034 application does not appear to use the term "casing," but does disclose the use of a "controlled release capsule." However, since such a capsule may not "change the physical characteristics of the mixture" contained therein, it may not fall under the patent-eligible claim of this USPTO example.

Claims DO NOT recite "casing", claims recite "contained in one or more complementing casings providing controlled delivery of the formulation to a subject". Claims have to be examined by the plain words of the claims in context of surrounding words. In re Gulack, 703 F.2d 1381, 1385 (Fed. Cir. 1983). Trivascular, Inc. V. Samuels, 812 F.3d 1056, 1061 (Fed. Cir. 2016).

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NOTE: The highlights and the text in side bar have been added by the Applicant.

Publications

In Re Urvashi Bhagat: One More Decision Denying Patent Eligibility of Nature-Based Product Claims

March 29, 2018

Urvashi Bhagat appealed the decision of the PTAB ("the Board") affirming the examiner's anticipation rejections and the rejection under Section 101 of multiple claims in application 12/426,034. The Federal Circuit affirmed the Board's decision in the recent *In re Urvashi Bhagat* nonprecedential opinion. The claims of this application were directed to lipid-containing formulations comprising omega-6 and omega-3 fatty acids. The '034 application stated that dietary deficiency or imbalance of these fatty acids might lead to a variety of illnesses, and that omega-6 and omega-3 fatty acids are naturally occurring in oils, butters, nuts, and seeds. The '034 application claimed ranges and ratios of the fatty acids and other limitations.

Claim 65 recited:

> *A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids from different sources, and wherein (1) omega-6 fatty acids are 4–75% by weight of total lipids and omega-3 fatty acids are 0.1–30% by weight of total lipids; or (2) omega-6 fatty acids are not more than 40 grams.*
>
> Other claims included specific amounts and/or ratios, additional components, sources of the lipids, and delivery methods.

Under Section 101, the examiner rejected the claims (and the Board agreed) as being directed to non-statutory subject matter, because the claimed fatty acid mixtures occur naturally in walnut oil and olive oil. The Patent Office did not provide a clear step-by-step analysis under Section 101, as required by its own guidelines, and merely offered a mixed and brief statement that the claimed "intermixture of lipids from different sources" is "structurally indistinct" from lipid formulations derived from a single source, as shown in the prior art. The examiner found that the claims were directed to natural products of walnut oil and olive oil, and that the additional limitations in the claims did not change the characteristics of the products, or add "significantly more" to the claims. The Applicant offered a number of arguments for patent eligibility but the court agreed with the Board.

The Applicant's arguments for patent eligibility included statements that the claimed "intermixture of lipids from different sources" does not occur in nature and that the properties of the claimed formulations from different lipid sources are different from the properties of natural products from a single source. The Applicant pointed to the specification describing that the claimed mixtures provide benefits of "synergy" and "avoid concentrated delivery of specific phytochemicals that may be harmful in excess." The Applicant further argued that the claimed mixtures of fatty acids from different sources were "structurally different" from the single-source walnut oil and olive oil. However, the Applicant apparently did not offer evidence to bolster this argument. The Applicant explained that while naturally occurring plants or their isolated lipids might be natural products, extracts and composites or mixtures are not natural products because the extraction processes required for obtaining edible oils from olives and walnuts transform the claimed lipids from natural products. However, the Board held that the arguments did not overcome the identity of the claimed products and the naturally occurring lipid profiles of walnut oil and olive oil. The Board cited the references showing the lipid content of natural walnut oil and olive oil, and pointed out that the claims included this lipid content. The Board stated that the specification did not distinguish the claimed omega-3 and omega-6 fatty acids, from the omega-3 and omega-6 fatty acids that exist in nature, and that the Applicant did not provide evidence of such

Overwhelming evidence including five scientific publications (Appx6650-6707) and four PHOSITA testimonies have been submitted that in nature omega-6/ omega-3 always occur with certain phytochemicals in configurations necessarily altered by manipulations, e.g. storing, extracting, mixing, encasing... E.g., Gotoh (Appx6696) evidences even changing ratios of omega-3 and omega-6 affect each other in oxidative stability. UBBr12, 16, 53, 59; UBRBr15-16. Op11-12 "Applicant has not shown [evidence] …" is false. Petition #23-24.

ASSOCIATED PEOP

Marina I. Miller, Ph.D.

ASSOCIATED INDUSTRIES

- Life Sciences

distinction. The court agreed that the Board properly found that Bhagat failed to show that the claimed mixtures were a "transformation" of the natural products, or that the claimed mixtures had properties not possessed by these products in nature.

The Applicant further argued that the claimed limitations of "dosage" and "casings providing controlled delivery" do not exist as natural products, that natural products cannot provide a controlled delivery or dosage because lipid profiles in nature are unpredictable and that walnut oil and olive oil are not "natural products," as they can be obtained only by treatment of natural products. Here, the court seems to rely on the anticipation section of the opinion for the analysis under Section 101. In the anticipation analysis, the court agreed with the Board that the terms "casing" and "dosage" do not provide patentability to the compositions because "the specification states that these claim elements are not limiting and does not describe any assertedly novel characteristics of these components or their formulations." The court also agreed that the claims were directed to fatty acids that occur in nature and "that the asserted claim limitations do not distinguish the claimed products and compositions from those shown in the cited references." Thus, the analysis under section 102 was apparently applied to the analysis under Section 101. However, as explained by the Supreme Court in *Mayo*, the analysis under section 101 is separate from the patentability analysis under sections 102 or 103. Here, the main claim appears to include limitations that are not nature-based or that add "significantly more" to the nature-based product, e.g., the limitations "dosage" and "casings providing controlled delivery" are not found in nature and natural counterpart products and the claimed mixture "avoids concentrated delivery of specific phytochemicals that may be harmful in excess."

Specification does NOT say these elements are not limiting. Petition #2-4. This is a falsity, promoted by PTO upheld by Federal Circuit. It is extremely distressing that Federal Circuit would do that.

Another rejected claim 102 recited specific ratios of polyunsaturated, monounsaturated, and saturated fatty acids. The Board observed that the servings of olive oil and walnut oil shown in the references cited by the PTO in the anticipation rejections contained omega-6 and omega-3 fatty acids in the amounts within the claimed ranges. The Board held that the "intermixture of lipids from different sources" does not distinguish the claims from natural products because the Applicant "has not provided adequate evidence that an oil from different sources would necessarily have a composition that is different from one from the same source, nor that a different source would necessarily impart characteristics to the formulation which were absent when a single source was used."

Rejection of Claim 102 is extremely improper. Claim 102 recites combination of ratios of fatty acids that are NOT known in nature. Examiner failed to cite a single product, even oil, that meets the ratios in Claim 102. Petition #26.

The Applicant also argued that claim 128 was distinguished from natural products, and was not anticipated based on the limitation that the compositions contain "nuts or their oils" obtained from "almonds, peanuts, and/or coconut meat." However, the Board held that admixture with other natural products of known compositions was not shown or stated to change the nature of the compositions, citing *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 131 (1948). The court simply agreed that the Board correctly held that "claim 128 does not avoid the rejection on the ground that the claims are directed to known natural products."

In nature "almonds, peanuts, and/or coconut meat" do not contain omega-6 and omega-3 in the claimed ratios and concentrations, and mixing almonds/ peanuts/coconut with claimed omega-6/omega-3 ranges alters use because of antioxidants in them. Petition #27.

Thus, the court concluded that substantial evidence supported the Board's findings and the rulings of unpatentability.

In re Urvashi Bhagat, Appeal No. 2016-2525 (Fed. Cir., March 16, 2018)
Mayo Collaborative Servs. v. Prometheus Labs., Inc., 566 U.S. 66 (2012)

NOTE: The highlights and the text in side bar have been added by the Applicant.

In re Urvashi Bhagat – The Slippery Slope of Natural Product Claims

Monday, March 19, 2018

ARTICLE BY

Warren Woessner

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patents4Life blog

Biotech, Food, Drug Intellectual Property Litigation / Trial Practice

Federal Circuit / U.S. Court of Spec. Jurisdiction

I will start out by recommending that you read all of MPEP 2106 – Patent Subject Matter Eligibility. I rarely admire PTO policy rules and guidelines, but this section reflects a lot of work, particularly in the standards for evaluating whether or not a claim is directed to a natural product. Please turn to Table at 2016(3). As I have written previously, the key sections – especially for natural products – are sections 2A and 2B.

Section 2A requires the Examiner to analyze whether or not the claim is directed to a natural product. If there is more than one claim element that could be a natural product, they are to be evaluated to see if they occur together in nature. If they do not, the components are each compared to its closest naturally occurring counterpart to see if any of the components is clearly not a product of nature. If none is, the nature-based combination is examined to see if the combination of components has "markedly different" characteristics due to the interactions in the combination.

This requires evidence of some change in physical or chemical properties if there is just one nature-based product in the claim or, alternatively some interaction between the natural products (if there is more than one). If this analysis leads to the conclusion that the nature-based component or components is significantly different from its/their natural state, it/they are not a product of nature and the inquiry stops. Also, carriers for a natural product that is the active ingredient, which are not themselves natural products, e.g., nanoparticles, will often have structural and physical characteristics that distinguish them from their closest natural counterparts (if there are any). Therefor a carrier can render a natural product patent-eligible. (These comments are based on Examples 3 and 4 in the Interim Examination Guidelines, May 4, 2016 Life Sciences Update).

If, however, the claim encompasses no more than a natural product or a simple combination thereof, and the marked difference is absent, the Examiner will subject the claim to the

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dreaded Step 2B analysis, in which to reach patent-eligibility, the claim must possess a further "inventive concept" that renders it "significantly more" and which cannot be satisfied by the product(s) of nature per se. While the PTO Guidelines state that the "inventive concept" question should not be decided on the basis of a ss. 102 or 103 analysis, the Board and the courts almost always do just that.

Now, at last, let's take a look at the Fed. Cir.'s affirmance of the Board's rejections In re Bhagat. Facially the claim is directed to a formulation comprising a dosage of specified amounts of omega-6 (o-6) and omega-3 fatty acids. One wrinkle in the claiming is the further limitation that the formulation is contained "in one or more complemented casings providing controlled delivery of the formulation to a subject."

Overwhelming evidence including five scientific publications (Appx6650-6707) and four PHOSITA testimonies have been submitted that in nature omega-6/omega-3 always occur with certain phytochemicals in configurations necessarily altered by manipulations, e.g. storing, extracting, mixing, encasing... E.g., Gotoh (Appx6696) evidences even changing ratios of omega-3 and omega-6 affect each other in oxidative stability. UBBr12, 16, 53, 59; UBRBr15-16. Op11-12 "Applicant has not shown [evidence]…" is false. Petition #23-24.

Well, there is no doubt that these fatty acids are natural products, especially since the inventor could not point to any marked difference between the individual acids and the mixture thereof and their naturally occurring counterparts. The Examiner had rejected the claims over a "nutritional composition for pediatric patients" as containing all the limitations present in the main claim. Other claims were rejected over the fatty acid profile of a serving of walnuts or olives. With respect to one claim, the inventor argued that the Examiner had not established that olives contained a group of carriers recited in the claim. Unfortunately, one of the carriers was sugar, and walnuts contain sugar.

Anticipation by olives and walnuts is wrong on the face because anticipation law requires same part to part relationship, the references do not disclose "intermixtures" and there are other issues with them. Petition #13-15.

In the 101 analysis, the Examiner abbreviated, if not conflated, the 2A and 2b; apart from the finding that o-6 and 04 fatty acids are directed to natural products, the Examiner found that

> "the additional limitations in the claims do not change the characteristics of the products [2A] or add 'significantly more' to the claims.' [2B]. That's a lot of law for about half a sentence, and made the court's s.101 arguments difficult to follow. In fact, the main claim used as representative do contain limitations that are not nature-based products, and impart at least functional structure to the claims. The claims require that the composition comprised a dosage of the fatty acids, contained in "one or more complementing casings providing controlled delivery of the formulation to a subject...."

While the court simply dismissed the claim element "casing" as meaning "any orally accepted form", in the anticipation section of the decision, court's reasoning was simply the term does not provide patentability to the compositions because the specification states that the term is not claim-limiting and, that it does not describe any novel characteristics of the components or their formulations. While this analysis may be appropriate in a patentability analysis under ss. 102/103, it should not be carried over into a s. 101 analysis.

Specification does NOT say these elements are not limiting. Petition #2-4. This is a falsity, promoted by PTO upheld by Federal Circuit. It is extremely distressing that Federal Circuit would do that.
Also, claims DO NOT recite "casing", claims recite "contained in one or more complementing casings providing controlled delivery of the formulation to a subject". Claims have to be examined by the plain words of the claims in context of surrounding words. Petition #3.

In the 101 analysis, the Applicant again argues that the claimed limitation "casings providing controlled delivery" are not natural products. So we are not in inventive concept territory yet, but are still evaluating whether or not the formulations are markedly different than the fatty acids as they occur in nature, e.g., in walnuts or olives. The court simply did not comment on this argument but certainly, Applicant's controlled release dosage form does not exist in nature and changes the characteristics of the acids as they occur in their natural state, in walnuts or olives. Unfortunately, applicant did not make this argument as clearly as I have with the benefit of hindsight, probably because the court was using facts largely derived from its anticipation ruling.

One of Applicant's better "markedly changed" arguments is that the claimed mixtures "avoid concentrated delivery of specific phytochemicals [also present in the olives or walnuts, I presume] that may be harmful in excess. The Board had argued that the entirely of the natural products finding should rest on the identity of the [recited] oils, to the naturally occurring lipid profiles in walnut or olive oil. The court agreed with the Board, simply stating that evidence supporting this argument was lacking.

The arguments were made VERY clearly and REAPEATEDLY with evidence, Federal Circuit disregarded them. "Preponderance of evidence is that nature cannot provide dosage (specified amount for once/ regular ingestion) or controlled delivery, because nature is random and unpredictable in lipid ratios and amount. (Appx5472-5474, Appx5480, Appx5703, Appx6054-6055, Appx7673, Appx7677-7678, Appx7875-7878). PTO has acknowledged "lipid components (e.g., amounts and ratios of omega-6/omega-3 fatty acids) present in any specific product of nature are not always the same." (Appx7783). Thus, there will be no specified amount for ingestion of omega-6/omega-3 in any given product of nature and there will be no controlled delivery. The very purpose of the inventions comprising process and composition of matter (dosages, casings, controlling delivery, intermixtures) is to solve the problem of deficiency, excess, or unpredictability in products of nature. (Appx7670-7673, Appx7677-7679)." UBBr50-52.

In the final paragraph, the court simply agrees with the Board that the fatty acids occur in nature and the "asserted claim limitations do not distinguish the claimed products and compositions from those shown in the cited references." Whether or not the oils occur in nature is part of the step 2A analysis, but the need to distinguish the products from the prior art is not even a requirement of the 2B analysis. Applicant deserved better than the courts use of the "naked" anticipation rejection to meet the standards for a judicial exception under s. 101.

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ANNEX J:

Open Letter to Andrei Iancu, Director, USPTO, and Sharon Prost, Chief Judge, Federal Circuit, April 27, 2018

(Addendums omitted since they are attached here in Annex I, and Annexes H, R, and AC)

April 27, 2018

Open Letter To Andrei Iancu, Director, US Patent and Trademark Office, and Sharon Prost, Chief Judge, United States Court Of Appeals For The Federal Circuit (CAFC) Regarding US Application 12/426, 034 and CAFC case #16-2525

Dear Sir/Madam,

Both USPTO and CAFC have done great injustice to us, 1000s of inventors and companies claiming “composition of matter”, and millions of Americans who suffer from chronic diseases associated with lipid imbalance.

117 million Americans suffer from chronic diseases associated with lipid imbalance, ~3 trillion annually is spent in US on treating those diseases, 99% of public cannot name lipids, nature is unpredictable in lipid content, and there is mass confusion and noise in the art. Lipids are in all foods, but added oils are a particular problem because they are concentrated extract absorbed differently than other foods. It is a perpetual problem continuing for centuries and expected to continue for centuries, unless solved as invented. Piecemeal patents will not solve the problem.

Our company Asha Nutrition Sciences, deeply understanding the flawed teachings in the art, invented lipid dosages contrary to prior art teachings, and filed for patents in 2009 because without patents economics do not work to turn the tide. USPTO mutilated our claims and disclosure, and **promoted falsities**, and misapplied the law across the board to deny patents, which falsities were copied by some other patent offices. We appealed to CAFC. CAFC **rubber-stamped USPTO falsities**, contrary to a large body of its own and Supreme Court precedents, and issued a disjointed evasive non-opinion, uncharacteristic and unexpected from the panel of judges and the 2nd highest seat of justice in the United States of America, the "most advanced country" in the world.

Main Issues:

Claims recite, "dosage of omega-6/omega-3" and "casings providing controlled delivery of the formulations", which nature cannot provide. The line of attack from USPTO and CAFC: mutilate the terms! Specification provides six tables and ~20 examples, where it emphasizes importance of dosages and that there is a rather sensitive dose-effect of omega-6 and omega-3 (changing by level of administrations and body stores). There is one statement in the Specification "any orally acceptable form" (meaning any food form), but the Specification does NOT say, "dosage means any amount." The falsity promoted by USPTO and upheld by CAFC is that "any orally acceptable form" means dosage is not limiting, **despite the six tables and ~20 examples teaching specific dosages, and that inventor and skilled persons provided testimony during prosecution that "dosage" means "specified amount for**

administration," and despite that claims recite "dosage" and "casings providing controlled delivery of the formulations" not "any orally acceptable form." As per CAFC and Supreme Court precedents, inventor's interpretation during prosecution and skilled person's testimony cannot be disregarded, and claims are examined by plain words of the claims.

By mutilating the terms "dosage of omega-6/omega-3" and "casings providing controlled delivery of the formulations" USPTO and CAFC alleged that claims are drawn to "products of nature" although claims also recite "intermixture of lipids from different sources," which by law is a structural limitation and a "composition of matter", patent eligible as per 35 USC § 101. Further, § 102-type analysis was applied under § 101, contrary to controlling law from Supreme Court in *Mayo* and *Alice*.

USPTO and CAFC also applied "anticipation" 35 USC § 102 rejections by mutilating and disregarding "dosage of omega-6/omega-3", "casings providing controlled delivery of the formulations", "intermixture of lipids from different sources," and prosecution disclaimers to "single source", even though anticipating reference must necessarily function as claimed, different from obviousness rejection under 35 USC § 103. They could not apply § 103 rejections because claimed subject matter is not obvious due to opposite teachings in the art.

There is a reason why § 103 has been legislated separately from § 102—to solve problems that are not well understood or critical but not solved. USPTO and CAFC wiped out the separation between §§ 101, 102, and 103, and the very purpose of the separations.

After the CAFC Opinion was published, several lawyers in the field unaffiliated with us also opined that the USPTO and Court had wronged us.

We have filed the enclosed Petition for Rehearing En Banc. The Petition includes annotated copies of the Opinion and the opinions issued by other lawyers. We hope it will provide us the long overdue justice. If we are unsuccessful at CAFC, we will appeal to Supreme Court.

During the nine years the application has been pending, 13.6 million (1.5 million in ~2 years the application has been pending at CAFC) Americans have died of associated diseases (http://www.cdc.gov/nchs/fastats/deaths.htm).

We request your attention so that further injustice can be avoided, and public can be provided with the solutions.

Sincerely,

Urvashi Bhagat

Chief Executive Officer

ANNEX K:

Petition for a Writ of Certiorari to the US Supreme Court, August 29, 2018 (case no. 18-277)

APPENDIX A	Federal Circuit Opinion March 16, 2018, **omitted** since it is attached here as Annex H
APPENDIX B	Patent Trial and Appeal Board Decision on Petition (Denying Review), August 16, 2016, **omitted**
APPENDIX C	Patent Trial and Appeal Board Decision on Request for Rehearing (Denying Rehearing), June 21, 2016, **omitted**
APPENDIX D	Patent Trial and Appeal Board Decision on Appeal, April 15, 2016, **omitted** since it is attached here as Annex G
APPENDIX E	Federal Circuit Order (Denying Rehearing), June 1, 2018, **omitted**
APPENDIX F	Statutes, **omitted**
APPENDIX G	Claims at Issue Below, **omitted** since those are attached here at the end of Annex A

No.

In the Supreme Court of the United States

URVASHI BHAGAT,

Petitioner,

v.

ANDREI IANCU, DIRECTOR, U.S. PATENT AND TRADEMARK OFFICE,

Respondent.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

PETITION FOR A WRIT OF CERTIORARI

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QUESTIONS PRESENTED

This petition presents a conflict between the incentive to invent, as the Constitution provides for, and the breadth of patent-eligible subject matter under 35 U.S.C. § 101. It has become difficult to recognize the line between patentable subject matter and non-patentable products of nature. This Court has made conflicting statements regarding that line.

In the case at hand, petitioner, a solo inventor, has invented new and useful lipid compositions that can improve the health of millions of Americans who suffer from chronic illness. Yet she is being denied a patent that would support her in bringing these beneficial inventions to market. This frustrates the purpose of the U.S. patent system.

This petition further presents the issue of holding the federal courts accountable in properly reviewing agency decisions.

The Questions Presented are:

1. a. Whether the Federal Circuit erred in finding petitioner's patent application claims unpatentable under 35 U.S.C. § 101 because the court failed to apply the correct patent-eligibility standard under this Court's conflicting holdings in *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948) and *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576 (2013).

b. Whether the Federal Circuit erred in finding petitioner's patent application claims unpatentable under 35 U.S.C. § 101 because the court did not apply the patent-eligibility standard set forth in *Myriad*.

2. Whether the Federal Circuit erred in affirming the USPTO's decisions under 35 U.S.C. §§ 101 and 102(b) because it failed to apply "meaningful review" to that decision, as required by the Administrative Procedure Act.

CORPORATE DISCLOSURE STATEMENT

Asha Nutrition Sciences, Inc. owns 100% of U.S. Patent Application No. 12/426,034, the patent application at issue. Asha Nutrition Sciences, Inc. has no parent company, and no publicly held corporation owns 10% or more of its stock. Petitioner Urvashi Bhagat is the applicant in the '034 application and is president of Asha Nutrition Sciences, Inc.

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The opinion of the court of appeals (Pet.App. 1a-14a) is reported at 726 Fed. Appx. 772. The opinion of the Patent Trial and Appeal Board (Pet.App. 23a-63a) is unreported.

JURISDICTION

The court of appeals issued its decision on March 16, 2018. A combined petition for panel rehearing and rehearing en banc was denied on June 1, 2018. Pet.App. 64a-65a. The jurisdiction of this Court is invoked under 28 U.S.C. § 1254(1).

STATUTORY PROVISIONS INVOLVED

1. 35 U.S.C. § 101 provides: "Inventions patentable. Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."[1]

2. 35 U.S.C. § 102(b) provides:

> A person shall be entitled to a patent unless—
>
> . . . (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States.[2]

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[1] 35 U.S.C. § 101 did not change under the Leahy-Smith America Invents Act (2011) ("AIA").

[2] The pre-AIA version of 35 U.S.C. § 102(b), set forth in the

STATEMENT

This case presents an instance in which an inventor has made and disclosed valuable inventions that apply new and useful discoveries to the solving of long-felt and critical public health problems. Chronic diseases affect millions of Americans. Petitioner, the inventor of U.S. Patent Application 12/426,034 (which claims priority to an April 21, 2008 filing date), has developed formulations that have the potential to ameliorate or alleviate the symptoms of many who suffer from chronic diseases. Nevertheless, petitioner has been denied the patent reward that this country's founders enabled to encourage and foster innovation.

The rejection of the claims pending in the '034 application, at issue here, appears to be, in part, a consequence of uncertainty in the proper application of 35 U.S.C. § 101. This case merits review to clarify the scope of patentable subject matter under 35 U.S.C. § 101 and of the incentive to innovate and to invest in and disclose innovations. Review of this case will also resolve some of the substantial doubt that uncertainty surrounding § 101 has cast on the validity and value of such patents.

Under the Court's interpretation of 35 U.S.C. § 101, "anything under the sun that is made by man" is eligible for patenting, provided that it meets other statutory requirements. *See Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980). The Court has determined that patentable subject matter does not include physical phenomena, laws of nature, and

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text, applies to this case.

abstract ideas. *See id.* The question of what falls within the category of physical phenomena, also referred to as "natural phenomena," remains difficult to answer. *See*, *e.g.*, *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 589-90 (2013). Petitioner seeks clarification from the Court on this issue.

A. Background

In this case, petitioner Urvashi Bhagat, motivated by the illness, suffering and premature death of her own mother, devoted herself to researching the relationship between diet and chronic illness. She focused on the role of lipids in health and disease. Lipids are a diverse class of over 100 distinct chemical compounds that are ubiquitous in nature and include, for example, fatty acids, cholesterol, steroids and certain vitamins. *See* Eoin Fahy *et al.*, *A comprehensive classification system for lipids*, 46 J. Lipid Res. 839, 843, 848-50, 854-55 (2005) (listing and describing classes of lipids). Lipids play many important biological roles, including being crucial cell membrane components, providing a source of energy to the organism, affecting protein function and involvement in gene regulation. *See id.* at 848, 850, 854-55; *see also* Fed. Cir. App. Appx0056. Lipids affect the activity of each other and their derivatives function as important hormones and chemical messengers that affect a broad range of physiological functions. *See* Fed. Cir. App. Appx0056.

Petitioner's research has focused on two subsets of lipids, the omega-6 and omega-3 families of fatty acids. Fed. Cir. App. Appx0056-Appx0057. Linoleic

acid (LA) is the precursor of the omega-6 family, and alpha-linolenic acid (ALA) is the precursor of the omega-3 family. *Id.* The bodies of mammals, including humans, cannot synthesize LA and ALA, but can synthesize the other omega-6 and omega-3 fatty acids from dietary LA and ALA. *Id.* Mammals must obtain LA and ALA from dietary sources. *Id.*

From about 1930 to about 1960, nutritional studies demonstrated that omega-6 fatty acids were active in growth and maintenance of skin health. Between 1964 and 1979, researchers developed awareness that arachidonic acid (AA) (an omega-6 fatty acid) metabolizes into prostaglandins and leukotrienes, involved in several disease processes associated with arthritis, asthma, atherosclerosis, thrombosis, tumor proliferation, and a variety of immune-inflammatory disorders. Therefore, high amounts of omega-6 were believed to promote pathophysiology. Ingestion of about 1% of daily calories as LA was considered to be optimal, and omega-3 fatty acids were believed to be beneficial and inhibit omega-6 activity by competitive metabolism. *See* Fed. Cir. App. Appx4263-Appx4269.

Experts believed that, for LA and ALA to be equally competitive, their intake should be in the ratio of 14:1, but that equality of competition may not be the criterion for optimal function. *See*, *e.g.*, Fed. Cir. App. Appx0231. The nutrition field recommended very low levels of omega-6 consumption. *See*, *e.g.*, *id.* Appx4448 (indicating upper limit of omega-6:omega-3 ratio of 2.32:1 and maximum omega-6 intake of 6.67 grams/day for a 2000 kcal diet). Thirty scientists ratified the

recommendation. *See id.* Appx4448-Appx4449.

Petitioner recognized, through her research in the early to mid-2000s on people who suffered from certain chronic conditions, that the recommended dosages and ratios were too low and that the prior art had greatly misunderstood the dose-effect of omega-6 fatty acids. The prior art held that a stepwise increase in omega-6 intake is associated with adverse health, such as an increase in tumorigenesis when the intake is in the range of 0.5-4.4% of calories. *See* Clement Ip *et al., Requirement of Essential Fatty Acid for Mammary Tumorigenesis in the Rat*, 45 Cancer Res. 1997-2001 (1985). Those skilled in the art therefore were not motivated to practice higher dosages of omega-6. *See* Fed. Cir. App. Appx4263-Appx4269 and Appx4446-Appx4449. Petitioner found, however, that higher intake of omega-6 was required to overcome adverse health conditions (for example, at least 11 grams per day or at least 5.82% of calories consumed). *See* Fed. Cir. App. Appx0082-Appx0087, Appx0089-Appx0090, Appx0092, Appx0093, Appx0096-Appx0097 and at Appx0083-Appx0085 (Table 20).

Petitioner also discovered that the deficiency of omega-6 potentiates certain mechanisms, such that sudden increases in omega-6 have an overflow effect, which can lead to myocardial infarction, strokes, infections, and physiological disturbances. *See* Fed. Cir. App. Appx0082-Appx0097 and Appx1346-Appx1347.

Petitioner also determined that the optimal amounts and ratios of omega-6 and omega-3 intake depend upon a subject's intake of other lipids such

as, for example, antioxidants, phytochemicals, and other fatty acids and on a subject's demographics. *See*, *e.g.*, *id.* Appx0057-Appx0058, Appx0060-Appx0061. She devised formulations that embodied these ratios and amounts, and has pursued patents directed to such formulations. "[T]he ratio between [omega]-6-to-[omega]-3 of 15–17:1 in diets is not the problem, the problem is the other factors that influence the metabolism of [omega]-6 and [omega]-3." *See id.* Appx7367.

Petitioner's claimed formulations, being mixtures of components from different sources, are formulated to provide certain amounts and ratios of certain components. At the same time, other components that are not desirable in large amounts or high concentrations become diluted as a consequence of mixing lipids from different sources. The formulations thus provide a dual advantage.

Subsequent to petitioner's research and patent application filings, several public health organizations advised higher omega-6 intake based on experimental results. For example, the American Heart Association advised that the consumption of at least 5% to 10% of energy from omega-6 polyunsaturated fatty acids reduces the risk of chronic heart disease relative to lower intakes. *See* Fed. Cir. App. at Appx0205-Appx0207, Appx4222-Appx4234. Other "results suggested that low concentrations (≤200 μM) of LA promote colorectal cancer cell growth, while high levels (≥200 μM) induce apoptosis of the colorectal cancer cells *in vitro*." *Id.* at Appx4291.

Therefore, prior to petitioner's invention of the

claimed lipid formulations, the person of ordinary skill in the art *could not have determined* and practiced the claimed suitable ratios and dosages of total omega-6 and omega-3 fatty acids for a subject. Those of ordinary skill in the art have testified to this effect. *See* Fed. Cir. App. Appx3860-3861, Appx3868-3869, Appx3850. Additionally, the public cannot solve this problem because lipids are unpredictable in their sources and less than 1% of Americans understand lipids. *See id.* Appx5703, Appx5472-5474, Appx6650-6668, Appx6670-6685, Appx7910. Thus the claimed subject matter is directed to solving a poorly understood problem and meeting a critical and long-felt, unmet need. It has great potential to protect and improve public health. *See id.* Appx6492-Appx6493, Appx6509-Appx6510, Appx6526-Appx6527.

B. Facts and procedural history

Petitioner filed U.S. Patent Application No. 12/426,034, the application at issue in this case, on April 17, 2009. *See* Fed. Cir. App. Appx0056-Appx0114. The '034 application claimed priority to three provisional applications, U.S. Provisional Nos. 61/046,747, filed April 21, 2008, 61/075,708, filed June 25, 2008, and 61/111,593, filed November 5, 2008. *Id.* Appx0056. Prosecution of the '034 application culminated in a final office action dated September 22, 2015. Claims 52, 61, 64, 65, 67-69, 73-75, 77, 78, 80, 82, 83, 90-105, 107-109, 111, 113-122, and 124-145 were then pending, of which claims 65, 91, 129, and 130 were independent. The Examiner rejected all claims as either drawn to non-statutory subject matter under 35 U.S.C. § 101, anticipated under 35 U.S.C. § 102(b) (pre-AIA), or

both. Petitioner filed an amendment on September 30, 2015 to put the claims in better condition for appeal, amending only dependent claim 117.

Independent claim 65 is reproduced below. The four independent claims 65, 91, 129, and 130 and all dependent claims are reproduced in the Appendix. *See* Pet.App. 68a-90a.

> 65. A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4: 1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids from different sources, and wherein
>
> (1) omega-6 fatty acids are 4-75% by weight of total lipids and omega-3 fatty acids are 0.1-30% by weight of total lipids; or
>
> (2) omega-6 fatty acids are not more than 40 grams.

Petitioner appealed *pro se* to the Patent Trial and Appeal Board. The Board issued its decision on April 15, 2016, affirming the Examiner's claim rejections. Pet.App. 23a-63a.

The Board relied on this Court's decisions in *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948) and *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576 (2013) in finding the claims read on patent-ineligible "products of

nature." Pet.App. 31a-34a. The Board rejected Appellant's contention that the claimed subject matter was patent-eligible. Pet.App. 32a-37a.

Petitioner filed a request for rehearing by the Board on June 14, 2016. The Board denied the request on June 21, 2016. Pet.App. 21a-22a. Petitioner filed a petition for supervisory review by the Chief Administrative Patent Judge of the Board on July 5, 2016 and a Notice of Appeal *pro se* to the United States Court of Appeals for the Federal Circuit on August 16, 2016. The Board dismissed the petition for lack of jurisdiction on September 30, 2016. *Id.* 15a-20a.

The Federal Circuit issued a non-precedential decision on March 16, 2018, affirming the Board's decision. *Id.* 1a-14a. The Federal Circuit had jurisdiction under 35 U.S.C. § 141(a). The court concluded substantial evidence supported the Board's conclusion "that the claims are directed to the omega-6 and omega-3 fatty acids that occur in nature and that the asserted claim limitations do not distinguish the claimed products and compositions from those shown in the cited references." Pet.App. 14a. The court also affirmed the Board's findings on anticipation. *Id.* 10a.

The court denied petitioner's petition for panel rehearing and for rehearing en banc on June 1, 2018. *Id.* 64a-65a.

REASONS FOR GRANTING THE PETITION

This case is an ideal vehicle for providing the clarification the patent and investment community require. At issue is how to determine whether

something is a product of nature under 35 U.S.C. § 101. This case embodies the need for further guidance because this application was rejected while patents that contain claims indistinguishable, on § 101 grounds, from the present case have issued previously (*see infra*). Clarification from the Court will enable the patent and investment communities to allocate their resources more efficiently by pursuing patents only on patent-eligible subject matter.

More specifically, the patent community and others lack a clear understanding of the boundaries of § 101 and how the statute is properly applied under *Funk Bros.* and *Myriad*, including within the life sciences generally. *See*, *e.g.*, Peter Lee, *The Supreme Court's* Myriad *Effects on Scientific Research: Definitional Fluidity and the Legal Construction of Nature*, 5 U.C. Irvine L. Rev. 1077, 1104-1110 (2015). Also, § 101 challenges have increased subsequent to the Court's series of § 101 decisions. According to one analysis, in the art unit in which the '034 application was prosecuted, the percentage of USPTO rejections that cite § 101 has almost tripled from the pre-*Bilski* period (just over 5%) to the post-*Alice* period (just under 15%).[3] *See* James Cosgrove, § 101 Rejections in the Post-Alice Era (March 7, 2017) (available at https://www.ipwatchdog.com/2017/03/07/101-rejections-post-alice-era/id=78635/ (last visited Aug. 27, 2018)).

The patent system promotes "progress by offering

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[3] *See Bilski v. Kappos*, 561 U.S. 593 (2009), *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347 (2014)

inventors exclusive rights for a limited period as an incentive for their inventiveness and research efforts." *See Diamond v. Chakrabarty*, 447 U.S. 303, 307 (1980); *see also In re Piasecki*, 745 F.2d 1468 (Fed. Cir. 1984) ("it states that advancement in the art is the overriding constitutional standard 'to be implemented by the Commissioner and the courts'"[4]). Congress has provided a patent system to "have a positive effect on society through the introduction of new products and processes of manufacture into the economy, and the emanations by way of increased employment and better lives for our citizens." *Chakrabarty*, 447 U.S. at 307 (quoting *Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470, 480 (1974)).

The current uncertainty in the patent community has a chilling effect, deterring the investment of work and resources in innovation when recoupment in the form of a patent is unclear. *See*, *e.g.*, Sen. Christopher Coons, *A Few Thoughts on the Supreme Court's Section 101 Jurisprudence* (2017) (available at http://www.ipwatchdog.com/2017/02/08/ thoughts-supreme-courts-section-101-jurisprudence/ id=78166/) (last visited Aug. 16, 2018) (discussing "the sheer amount of ambiguity that the developing Section 101 jurisprudence is creating"). Additional guidance will provide confidence in, and thereby promote, such investment. The public will benefit from the inducement to innovate. Particularly in this case, patent protection is necessary to nurture this innovation because it cannot be heard above the

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[4] Referring to *Comm'r of Patents v. Deutsche Gold-und-Silber-Scheideanstalt Vormals Roessler*, 397 F.2d 656, 665 (D.C. Cir. 1968).

noise.

Also at issue is a just outcome in the Federal Circuit that can only be obtained by meaningful review of the Board's decision.

A. *Myriad* and *Funk Bros.* articulate conflicting standards of patent-eligibility

1. 35 U.S.C. § 101

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101 (2018).

This Court has construed "'manufacture' in § 101 in accordance with its dictionary definition to mean 'the production of articles for use from raw or prepared materials by giving to these materials new forms, qualities, properties, or combinations, whether by hand-labor or by machinery.'" *Diamond v. Chakrabarty*, 447 U.S. 303, 308 (1980) (quoting *American Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1, 11 (1931)). The Court further has endorsed construing "composition of matter" "to include 'all compositions of two or more substances and . . . all composite articles, whether they be the results of chemical union, or of mechanical mixture, or whether they be gases, fluids, powders or solids." *Id.* at 308. The Court has found that a "broad construction" of the patent laws conforms with Thomas Jefferson's vision and the history of the patent system generally. *See id.* at 308-09 (stating, in part, the Patent Act of 1793 "embodied Jefferson's

philosophy that 'ingenuity should receive a liberal encouragement'").

Section 101 nevertheless has limits. "The laws of nature, physical phenomena, and abstract ideas have been held not patentable." *Id.* at 309. For example, one may not patent "a new mineral discovered in the earth." *Id.* at 309.

2. Patent-eligibility under *Funk Bros.*

In *Funk Bros.*, the Court held not patent-eligible a mixture of different species of naturally-occurring bacteria. *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 128 n.1, 130, 132 (1948).

Each species of bacteria was useful in planting and growing a subset of crops, and each had been sold separately because each species inhibited the others. *See id.* at 128-130. The inventor discovered certain strains of each bacterium did not inhibit certain strains of the other species, and could "be isolated and used in mixed cultures." *Id.* at 130. The inventor patented combinations of the non-inhibitory bacteria that could be used together on all of the crops. *See id.* Thus, a single, multi-function combination bacterial culture replaced multiple, single-function cultures. The claimed mixture provided commercial advantages and convenience to farmers and agricultural suppliers. *Id.* at 131-132.

The Court reasoned that the qualities of the bacteria at issue were "manifestations of laws of nature, free to all men and reserved exclusively to none." *Id.* at 130. If "there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end." *Funk*

Bros., 333 U.S. at 130. Yet the "aggregation of species fell short of invention within the meaning of the patent statutes." *Id.* at 131. Although devising such a mixture represented a "discovery" and provided an "advantage," no species acquired a different use and each species had "the same effect it always had" and "perform[ed] in their natural way." *Id.* at 131. Once the patentee had discovered the non-inhibitive quality of the different strains, "the state of the art made the production of a mixed inoculant a simple step," and thus "was not the product of invention."

While the statutory precursor to the current § 101 governed both patent-eligibility and novelty at the time *Funk Bros.* was decided, the Court has treated this case as a patent-eligibility case that contributes to defining the contours of the modern § 101. *See, e.g.*, *Chakrabarty*, 447 U.S. at 310 (citing *Funk Bros.* in support of the proposition that § 101 has "limits").[5]

3. Patent-eligibility under *Myriad*

In *Myriad*, the Court held that "genes and the information they encode are not patent eligible under §101 simply because they have been isolated from the surrounding genetic material." *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 596 (2013). On the other hand, cDNA is

[5] The statute at the time, titled "Inventions patentable," referred to obtaining a patent for invention or discovery of "any new and useful art, machine, manufacture, or composition of matter, or any new and useful improvements thereof," that was, for example, "not known or used by others in this country, before his invention or discovery thereof." 35 U.S.C. § 31 (1946).

patent-eligible because it "is not naturally occurring." *Id.* at 594. Rather, cDNA is a synthetic partial copy of gene DNA that contains the same protein-encoding exons as the corresponding gene DNA but not the gene's non-coding introns. *See id.* at 594. "cDNA retains the naturally occurring exons of DNA, but it is distinct from the DNA from which it was derived. As a result, cDNA is not a 'product of nature,'" with the exception of cDNA that corresponds to a stretch of DNA that contains no introns. *Id.* at 595.

At issue in *Myriad* were the BRCA1 and BRCA2 genes, mutations in which are associated with breast cancer. Specifically, the patentees had claimed isolated copies of the DNA corresponding to the genes, removed from the cell, and cDNAs that comprise the BRCA1 or BRCA2 exons spliced together, omitting the introns present in the naturally occurring genes. "Myriad did not create or alter any of the genetic information encoded in the BRCA1 and BRCA2 genes" or "create or alter the genetic structure of DNA," so patent claims to "naturally occurring, isolated DNA segments" were considered not sufficiently removed from the natural product. *Myriad*, 569 U.S. at 590. "Myriad did not create anything. To be sure, it found an important and useful gene, but separating that gene from its surrounding genetic material is not an act of invention." *Id.* at 591. Thus, simply discovering something in nature and isolating it does not qualify for patent-eligibility because it is not inventive.

In contrast, cDNA is patent-eligible because it is "something new" that "is not naturally occurring." *Myriad*, 569 U.S. at 594, 595. The Court reached

this conclusion despite the fact that preparing cDNA was routine at the time the patents at issue in *Myriad* were filed (*circa* 1994). *See*, *e.g.*, Benjamin Lewin, *Genes IV* 456 (1990) ("synthesiz[ing] a duplex DNA from an mRNA" "is especially easy for mRNAs that carry a poly(A) tail at the 3' end," from which can be prepared "a cDNA clone").

This conclusion, however, directly conflicts with *Funk Bros.*, which reasoned that a "simple step" that leads from the discovery to the claimed subject matter did *not* make the claimed subject matter "the product of invention" or patent-eligible. *See Funk Bros.*, 333 U.S. at 132.

Further, the information in cDNA is "dictated by nature," as the Court recognized. *See Myriad*, 569 U.S. at 595. In sum, no inventiveness was required to prepare BRCA1 or BRCA2 cDNA once the BRCA1 and BRCA2 genes were isolated.

The "rule against patents on naturally occurring things is not without limits" because "'all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas,' and 'too broad an interpretation of this exclusionary principle could eviscerate patent law.'" *Id.* at 589-90 (quoting *Mayo Collaborative Servs. v. Prometheus Labs, Inc.*, 566 U.S. 66, 71 (2012)). Thus, "patent protection strikes a delicate balance between creating 'incentives that lead to creation, invention, and discovery' and 'imped[ing] the flow of information that might permit, indeed spur, invention.'" *Myriad*, 569 U.S. at 590 (quoting *Mayo*, 566 U.S. at 92).

4. *Funk Bros.* and *Myriad* produce conflicting results

Funk Bros. and *Myriad* each provide guidance for determining whether, when a natural product is used to make a new product, the new product is sufficiently different from the natural product to be patent-eligible under section 101. The guidance each provides, however, yields conflicting results.

Myriad indicates that the new product, to be patent-eligible, cannot be identical to the natural product.

The application of *Myriad*'s reasoning to the facts in *Funk Bros.* leads to a different outcome than the Court reached in *Funk Bros.* Specifically, the Court would have recognized that the combinations of bacterial species at issue were in fact patent-eligible because such combinations represented the application of a discovery to yield "something new" that was "not naturally occurring," specifically, a mixture not found in nature of different bacterial species. *See Myriad*, 569 U.S. at 594, 595. The Court in *Funk Bros.* in fact recognized the bacterial combinations or mixtures provided "an important commercial advance." *Funk Bros.*, 333 U.S. at 132.

In *Funk*, the inventor discovered certain bacterial properties and applied this discovery to make a new and useful combination of natural products. In *Myriad*, the inventors discovered two BRCA genes and applied this discovery to make a new and useful product (cDNA). In both cases, the claimed subject matter functioned naturally (the cDNA in *Myriad* encodes the same genetic information as the genomic DNA and otherwise functions the same as naturally

occurring DNA). As Justice Frankfurter stated, the claimed combination of bacteria was a patentable "invention" because the claimed "mixture does in fact have the new property of multiservice applicability." *See Funk Bros.*, 333 U.S. at 135 (concurring on other grounds). Further, Justice Frankfurter considered the patent-eligibility of the claimed composite to have been validated by the majority's statement that "if there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end." *Id.* at 135.

Similarly, application of the reasoning in *Funk Bros.* to the facts of *Myriad* would lead to a finding that both Myriad's genomic DNA and the corresponding cDNA are not patent-eligible. In *Funk Bros.*, the Court reasoned that the inventor's discovery of the bacterial qualities underlying the invention was "no more than the discovery of some of the handiwork of nature," and therefore "is not patentable." *Funk Bros.*, 333 U.S. at 131. The inventor's application of that discovery to devise a combination of different bacteria species "is hardly more than an advance in the packaging of the inoculants." "[T]hat aggregation of species fell short of invention within the meaning of the patent statutes." *Id.* at 131.

Applying this reasoning to *Myriad*, the identification of the BRCA genes was a discovery of some of the "handiwork of nature," so those genes isolated from the genome would not be patent-eligible under *Funk Bros.* *Id.* at 131.

Further, cDNA prepared using the knowledge of the BRCA genes would not represent a patent-

eligible "invention or discovery," as *Funk Bros.* would require, because it was a "simple step" to prepare the claimed BRCA cDNAs from the corresponding genomic DNA. *See id.* at 132. In sum, no inventiveness was required to prepare BRCA1 or BRCA2 cDNA once these genes were isolated. Thus, the application of *Funk Bros.* to the facts in *Myriad* would have led to BRCA genomic *and cDNA* being held unpatentable.

B. The court below erred in finding petitioner's claimed formulations not patent-eligible

Myriad articulates the proper patent-eligibility standard under 35 U.S.C. § 101. The Board and Federal Circuit erred in finding the pending claims patent-ineligible under *Myriad* because they applied the wrong standard under 35 U.S.C. § 101.

1. Claim construction

Each element contained in a patent claim is deemed material to defining the scope of the patented invention. *See Warner-Jenkinson Co., Inc. v. Hilton Davis Chemical Co.*, 520 U.S. 17, 29 (1997).

"A claim in an unexpired patent that will not expire before a final written decision is issued shall be given its broadest reasonable construction in light of the specification of the patent in which it appears." 37 C.F.R. 42.200(b). The Court has endorsed the Patent Office's adoption of the broadest reasonable construction standard. *See Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2146 (2016). "While the broadest reasonable interpretation standard is broad, it does not give the [b]oard an unfettered license to interpret the words in a claim

without regard for the full claim language and the written description." *In re Power Integrations, Inc.*, 884 F.3d 1370, 1375 (Fed. Cir. 2018) (holding that the "board's claim construction here was unreasonably broad and improperly omitted any consideration of the disclosure in the specification").

"The ultimate issue of the proper construction of a claim should be treated as a question of law" but "subsidiary factfinding is sometimes necessary." *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 838 (2014) (citing *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 378, 388, 390 (1996). "[W]e review the Board's ultimate claim constructions de novo and its underlying factual determinations involving extrinsic evidence for substantial evidence." *Microsoft Corp. v. Proxyconn, Inc.*, 789 F.3d 1292, 1297 (Fed. Cir. 2015) (citing *Teva*, 135 S. Ct. at 841-42 and "our review of Board determinations) (overruled on other grounds); *see also Dickinson v. Zurko*, 527 U.S. 150, 152, 161, 164 (1999) ("A reviewing court reviews an agency's reasoning to determine whether it is 'arbitrary' or 'capricious, or, if bound up with a record-based factual conclusion, to determine whether it is supported by 'substantial evidence.'"[6]).

Independent claims 65 and 91 and their dependent claims recite formulations that comprise "an intermixture of lipids from different sources." Pet.App. 69a, 73a. Independent claims 129 and 130 recite formulations that require "an intermixture of fatty acids from different sources." *Id.* 86a. The

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[6] The court set forth its reasoning in view of the Administrative Procedure Act, 5 U.S.C. § 706. Pet.App. 66a.

plain language of the claims thus requires a formulation that contains components that come from different sources. The '034 application instructs that "[i]n some embodiments, synergy among complementing nutrients from different sources may be incorporated. Furthermore, using different sources avoids concentrated delivery of specific phytochemicals that may be harmful in excess." Fed. Cir. App. Appx0062.

The specification indicates "sources" means seeds, nuts, fish, and other natural products, and oils derived therefrom. *See*, *e.g.*, Fed. Cir. App. Appx0061 (stating that "nuts and seeds" "are one of the richest sources of natural nutrients") and Appx0069 (describing compositions that "were made up of a variety of oils, nuts and seeds").

> (a) The decisions below incorrectly construed the claims as "product-by-process" claims, thereby improperly reading the limitation "intermixture . . . from different sources" out of the claims

The Board construed the claim term "intermixture" to refer to a process, and thus construed the claims as product-by-process claims not limited by the recited process. Consequently, it considered any single-source composition, such as walnut oil alone, to read on any of the claims if the single-source composition met the other limitations of that claim, such as fatty acid ratios. Pet.App. 29a-31a.

The Federal Circuit affirmed the Board's decisions on unpatentability under § 101 but did not directly address the product-by-process issue or

claim construction generally, and did not state explicitly whether it adopted the Board's construction or provide related reasoning. Pet.App. 10a-14a. Petitioner therefore concludes the court below adopted the Board's construction and supporting reasoning.

It was error to construe the claims as product-by-process claims. The claims are properly construed as standard composition claims and not as product-by-process claims. Strikingly, the decisions below provided no reasoning to support a product-by-process construction. They did not point to a recitation of process steps in any of the claims, or even to a verb suggesting a process step is required. *Cf. Andersen Corp. v. Fiber Composites, LLC*, 474 F.3d 1361, 1371 (Fed. Cir. 2007) (stating that the claims under consideration "do not contain an explicit process-based limitation"). Notably, the term "intermixed" can be construed as a structural limitation rather than a process limitation. *See In re Garnero*, 412 F.2d 276, 279 (C.C.P.A. 1969) (listing "intermixed" as one of a number of similar terms, such as "etched and "welded," that have been "held capable of construction as structural, rather than process, limitations").

The Board also did not point to any disclosure or requirement in the specification or prosecution history for a specific process for preparing mixtures of lipids or fatty acids. *Cf. Andersen Corp.*, 474 F.3d at 1371 (where the claim does not recite a process-based limitation, the court "look[s] to the specification and the prosecution history" "to determine whether the claim language should be construed as containing any such limitation").

To the contrary, the specification supports construing "intermixture" as a structural limitation and not as a product-by-process limitation. For example, the specification states "[s]ome compositions may include two or more of: almond oil (2%-36%), anhydrous butter oil (2%-36%), coconut oil (0%-8%), corn oil (1%-24%), flaxseed oil (0%-8%), mustard oil (0%-8%), olive oil (2%-36), palm oil (0%-2%), peanut oil (4%-72%), pumpkin seeds oil (1%-24%), safflower oil (high oleic) (2%-60%), soybean lecithin (0%-4%), sunflower oil (high oleic) (4%-72%), and/or walnut oil (2%-36%)." Fed. Cir. App. Appx0081. The resulting formulation's composition necessarily differs from natural products. In fact, Petitioner provided evidence in the form of expert declarations teaching that "when lipids from different sources are intermixed, the resulting mixture will *necessarily* have different physical and chemical properties from a 'single' source." Pet.App. 30a; *see also* Fed. Cir. App. Appx7230-Appx7236, Appx7239-Appx7240. This follows from the fact that different sources have different compositions. *See*, *e.g.*, Fed. Cir. App. Appx0063-Appx0064 (listing oils and their nutrient components); *see also* Fed. Cir. App. Appx5703, Appx5472-5474, Appx6614-6622, Appx6650-6685.

2. The inconsistency between *Funk Bros.* and *Myriad* caused the court below to apply the wrong standard under 35 U.S.C. § 101

Owing to the tension between the *Funk Bros.* decision's constricted patent-eligibility standard and the *Myriad* decision's broader patent-eligibility standard that more closely comports with the founders' vision, the Federal Circuit, which adopted

each point of the Board's reasoning either explicitly or implicitly, did not apply a correctly articulated standard under § 101. *Funk Bros.* requires both that the claimed subject matter not be found in nature and, beyond that, more than a "simple step." *Myriad* requires no more than that the claimed subject matter be "new" and not found in nature. It reserves additional requirements for evaluation under other provisions of the patent statute. *See Myriad*, 569 U.S. at 595 n.9. ("We express no opinion whether cDNA satisfies the other statutory requirements of patentability."). Surprisingly, the Federal Circuit did not cite *Myriad* in its opinion. The Court should grant the present petition in order to clarify the proper standard.

The Federal Circuit adopted explicitly or implicitly the reasoning "that the claims are directed to natural products of walnut oil and olive oil, and that the additional limitations in the claims do not change the characteristics of the products, or add 'significantly more' to the claims." Pet.App. 11a.

This was error. All of the pending claims require a "dosage" of "omega-6 and omega-3 fatty acids" or a "dosage" of "omega-6 fatty acids." Pet.App. 68a-90a. All of the claims require a "formulation" that is "contained" in at least one "casing providing controlled delivery of the formulation to a subject." *Id.* All of the claims require that the recited casing comprise an "intermixture of lipids from different sources" or "intermixture of fatty acids from different sources." *Id.* Even if the claims required only one of these non-naturally occurring elements, such as a casing or a dosage, the resulting subject matter would fall outside the scope of natural products

under *Myriad*. That the claims require all of a dosage, a formulation contained in a casing, controlled delivery of the formulation to a subject, and an intermixture from different sources only reinforces the conclusion.

To the extent *Funk Bros.* requires a demonstration that the claimed subject matter adds 'significantly more' to the claims, the Court should hold that *Myriad* has implicitly overruled this requirement. *Myriad* indicates that, as long as the claimed subject matter is new and does not occur in nature, it is patent-eligible. This reasoning forms the foundation for the *Myriad* Court's finding that the BRCA1 and BRCA2 cDNA is patent-eligible while the corresponding genomic DNA is not. The Court did not reason that the cDNA adds 'significantly more' than that which is present in the corresponding genomic DNA. In fact, the Court acknowledged the cDNA does *not* add significantly more. Rather, it contains the same genetic information as the genomic DNA. The claimed genomic and cDNA differed only in that cDNA does not occur in nature. Similarly here, formulations in casings, for example, do not occur in nature. The Court held in *Myriad* that § 101 does not require more. *See Myriad*, 569 U.S. at 594-95.

The Federal Circuit agreed with the Board "that the Applicant has not shown that the claimed mixtures are a 'transformation' of the natural products, or that the claimed mixtures have properties not possessed by these products in nature." Pet.App. 14a. This reasoning ignores the "dosage" and "casing providing controlled delivery of the formulation to a subject" limitations, as well as

the "intermixture" limitation. A formulation contained in a casing simply does not occur in nature. Thus, it has properties not possessed by natural products. Under *Myriad*, the degree of difference between what the court considers natural products and the claimed formulations is not at issue in determining whether subject matter is a natural product, *contrary to the reasoning in Funk Bros.*

The court affirmed the Board's conclusion "that the claims are directed to the omega-6 and omega-3 fatty acids that occur in nature, and that the asserted claim limitations do not distinguish the claimed products and compositions from those shown in the cited references." Pet.App. 14a. This is error for the same reasons as set forth immediately above. In short, "casing providing controlled delivery of the formulation to a subject," "dosage," and "intermixture" of fatty acids or lipids distinguish the claimed subject matter from omega-6 and omega-3 fatty acids by themselves.

The court explicitly or implicitly rejected petitioner's argument "that the claimed 'intermixture of lipids from different sources' does not occur in nature." Pet.App. 11a. For reasons set forth above, the court erred in rejecting this argument. The court's analysis relies on construing the claims as product-by-process claims, contrary to their plain language and the guidance provided in the specification. It is error to ignore claim limitations when construing claims. *See Warner-Jenkinson Co., Inc. v. Hilton Davis Chemical Co.*, 520 U.S. 17, 29 (1997) (stating that "[e]ach element contained in a patent claim is deemed material to

defining the scope of the patented invention").[7] Further, Petitioner provided evidence in the form of an expert declaration teaching that "when lipids from different sources are intermixed, the resulting mixture will *necessarily* have different physical and chemical properties from a 'single' source." Pet.App. 30a; *see also* Fed. Cir. App. Appx7230- Appx7236, Appx7239- Appx7240. Thus, an "intermixture . . . from different sources" differs from what is found in nature.[8]

Consequently, such a mixture differs from "a new mineral discovered in the earth" (*Chakrabarty*, 447 U.S. at 309) at least because the claimed intermixtures are not identical to any single natural product, for the reasons stated. Even assuming, without conceding, that sunflower oil and coconut oil are natural products, a mixture of the two simply "is not naturally occurring." *See Myriad*, 569 U.S. at 595.[9] Like the cDNA in *Myriad*, it is "unquestionably" "something new."

Importantly, even if "intermixture" is properly

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[7] The rule applies generally, though stated in *Warner-Jenkinson Co.* with respect to claim scope under the doctrine of equivalents.

[8] For example, sunflower oil can have 2.652 grams of oleic acid per tablespoon and coconut oil can have 0.789 grams of oleic acid per tablespoon. *See* Fed. Cir. App. Appx0063 (Table 2). A mixture of 1 tablespoon each will have an intermediate concentration of oleic acid (about 1.7 grams per tablespoon).

[9] Petitioner maintains that oils derived from, for example, olive oil and walnut oil, are not natural products because the extraction processes used to make such oils cause chemical and physical changes in the oil constituents, resulting in a composition that is not found in nature. *See* Fed. Cir. App. Appx6614-6622, Appx6650-6685.

construed as a product-by-process limitation, this construction affects only the scope of the formulation itself. It does not affect the limitation that the formulation is contained in a casing providing controlled delivery of the formulation to a subject or that the formulation comprises a dosage of the recited fatty acids. Yet the court below ignored these limitations, contrary to binding precedent.

Specifically, in addressing anticipation, the court stated that "[t]he Board found that the 'casing' and 'dosage' terms do not impart patentability to the claimed compositions, and we agree, for the specification states that these claim elements are not limiting, and does not describe any assertedly novel characteristics of these components or their formulations." Pet.App. 6a.

The court's reasoning that "these claim elements are not limiting" in evaluating anticipation was error, and it was error to apply this reasoning in its § 101 analysis. This reasoning misrepresents or fails to appreciate that the specification does not state that these claim elements are not limiting, and because it impermissibly reads limitations out of the claims. *Warner-Jenkinson Co.,* 520 U.S. at 29.

As the court noted in support of its finding, the specification states "'the compositions comprising the lipid formulation disclosed herein may be administered to an individual by any orally accepted form.'" Pet.App. 6a (referring to the passage that corresponds to Fed. Cir. App. Appx0065). First, the quoted language is preceded by "[i]n some embodiments," so it does not apply to all embodiments, such as the embodiments recited in

the claims. In any event, this cannot reasonably be understood to mean that the claim limitation "casings," or containers, does not limit the claimed subject matter to formulations that are contained in a container. Moreover, the application discusses specific kinds of containers that can be used to deliver the formulations; these would be within the scope of the "casings" limitation. Fed. Cir. App. Appx0066 (referring to "a gelatinous case, a vial, a pouch or a foil"). Petitioner presented these arguments to the Federal Circuit. *See* App. Br. 29-30. Furthermore, petitioner's patent application specification expressly states that "[i]t is intended that the following claims define the scope of the disclosure and that methods and structures within the scope of these claims and their equivalents be covered thereby." Fed. Cir. App. at Appx97. All of this points to "casings" limiting the claims, contrary to the findings below.

Further, the person of ordinary skill in the art would have understood the term "dosage" to refer to "specified amount to ingest at one time or regularly during a period of time," which definition was submitted to the PTO during prosecution and was affirmed by the testimony of skilled persons, as petitioner argued to the Federal Circuit. *See* App. Br. 41-42, 44.

The court acknowledged petitioner's argument "that the claimed limitations of 'dosage' and 'casings providing controlled delivery' do not exist as natural products. The Applicant states that natural products cannot provide a controlled delivery or dosage because lipid profiles in nature are unpredictable," but implicitly rejected this reasoning. Pet.App. 11a.

For the reasons stated above, it was error to ignore these claim limitations in evaluating the claims under § 101.

3. No preemption

The scope of patentability must be limited to avoid the "considerable danger that the grant of patents would 'tie up' the use of" "basic tools of scientific and technological work" and thereby 'inhibit future innovation premised upon them.'" *Myriad*, 569 U.S. at 589. The formulations of the present claims do not pose a danger of such tying up.

In *Myriad*, the Court recognized that patent claims that encompass genes for breast cancer could preclude basic medical and scientific research that could yield, for example, more effective treatments for breast cancer. Thus, such claims could thwart rather than promote the progress of science. Unlike the *Myriad* claims that were directed to genomic DNA, which is not materially changed from the corresponding DNA as it is found inside the cell, the claims at issue here encompass only non-naturally occurring *combinations* of materials that are contained in a non-naturally occurring casing and that constitute a non-naturally occurring dosage of certain fatty acids. These claims do not preclude basic research on, or use of, any of the individual components of the claimed formulations. For example, even if walnut oil were properly considered a natural product and a component of the clai formulations, the claims do not encompass walnut oil itself. Were these claims to issue, they would not preclude anyone from making, using, selling, offering for sale, or importing walnut oil. Thus, the

reasons to exclude basic tools from patent eligibility do not apply to the present claims.

4. The present claims are not distinguishable on § 101 grounds from other issued patents that claim lipid formulations

The USPTO considers compositions that contain naturally occurring lipids to be patent-eligible. Petitioner has identified several such patents in non-exhaustive searches. U.S. Patent No. 5,198,250 (issued March 30, 1993) claims compositions that comprise "at least one lipid species containing at least one short chain monounsaturated fatty acid selected from the group consisting of C16:1n-7, C16:1n-6, C16:1n-5 C16:1n-7, C16:1n-6, C16:1n-5, C16:1n-4, C16:1n-3, C14:1n-5, C14:1n-4, C14:1n-3, and C12:1n-3 . . . present in said composition in amounts sufficient to improve" metabolic processing of lipids in an animal. *See* '250 patent 26: 20-30 (claim 1). The recited fatty acids "occur naturally." *See*, *e.g.*, *id.* at 9: 18-21. For example, C16:1n-7 occurs in olive and cottonseed oils, *inter alia*, and C14:1n-5 occurs in animal fat. *See id.* at 9: 24-34.

U.S. Patent No. 6,183,796 (issued Feb. 6, 2001) claims compositions produced, for example, by heating "isolated lower limbs of cattle to liquify the fat contained therein to produce an oil" and "[r]ecovering the oil to provide a natural lipid composition enriched in C14:1 monounsaturated fatty acid." *See* '796 patent at 5: 30-35 (claim 1, reciting the process) and at 6: 33-34 (claim 13, directed to "[l]ipid compositions produced by the method of any of" the preceding claims).

U.S. Patent No. 7,759,507 (issued July 20, 2010)

claims a "lipid system comprising naturally occurring oils" wherein the recited oils are present in certain ratios. *See* '507 patent at 24: 36-42 (claim 1). The claim contains no additional limitations. *See id.*

These issued patents establish, contrary to the decisions below, that compositions that contain certain naturally occurring lipids, without further limitation other than amounts or ratios, qualify as patent eligible subject matter. It follows, *a fortiori*, that the claims at issue here, which likewise require certain lipids or fatty acids derived from different sources and present in certain amounts and ratios, and further require a casing and a dosage of one or more fatty acids, also qualify as patent eligible.

5. Additional guidance in applying § 101 will benefit inventors, investors, USPTO, and the lower courts.

Increased certainty in the patent-eligibility standard will permit the courts and patent office to accurately apply the standard and not bar patent-eligible claims from issuing or from being enforced. It will also encourage and promote efficient investment of time, effort, and resources in innovation because the relevant parties will have greater understanding of what to expect. Patent protection will also nurture innovation by small entities as they try to compete with better-funded entities. These outcomes ultimately will benefit the public because resources will be employed more efficiently.

C. The Federal Circuit's decision should be vacated and remanded for failure to meaningfully review the Board's decision.

1. "Meaningful review" required

When a court reviews an agency's decision, "the Court has stressed the importance of not simply rubber-stamping agency fact-finding." *Dickinson v. Zurko*, 527 U.S. 150, 162 (1999) (citing *Universal Camera Corp. v. NLRB*, 340 U.S. 474, 490 (1951)). "The APA requires meaningful review." *Id.*

2. No meaningful review of claim construction

The Federal Circuit affirmed the Board's decision in all respects. Pet.App. 2a. Claim construction played a key role in the Board's analysis. As discussed above, the Board addressed whether the claims are properly construed as product-by-process claims. Pet.App. 29a-31a. The Board's decision that the claims are product-by-process claims permitted it to ignore the claims' requirement for "an intermixture of lipids from different sources." It thus found the claims invalid under § 101 for reading on a single lipid source, walnut oil, which it characterized as a "product of nature." Pet.App. 31a-37a. It also relied on the product-by-process construction to find the claims invalid as anticipated by "Olives and 'Olives Nutrient Analysis'" (Pet.App. 50a-57a) and, independently, by "Walnuts and 'Walnut Nutrient Analysis (Pet.App. 57a-62a).

Petitioner contested the product-by-process construction on appeal. App. Br. at, e.g., 15-16, 18, 64. Yet the Federal Circuit did not address claim construction generally or the product-by-process construction specifically in its review of the Board's decision. The court's opinion does not refer to claim construction or claim interpretation except in a single reference to indicate that the "broadest

reasonable interpretation" standard applies. Pet.App. at 3a. Although the court recognized that "the Board's legal determinations receive de novo review," Pet.App. at 3a, it did not apply de novo or any other review to these issues.

The absence of a meaningful analysis or discussion of this contested and significant issue evidences the court's failure to meaningfully review an issue that petitioner contested and the Board decided. Consequently, the Court should vacate the Federal Circuit's decision and remand to require a determination of the proper construction of the claims at issue.

The outcome of this case would be reversed at least for independent claim 91 and its dependent claims if, on remand, it were determined that the claims are not properly construed as product-by-process claims, as argued above. Only a single reference, the "serving of walnuts as reported in the Walnut Nutrient Analysis," was found to anticipate claim 91, and, by extension, its dependent claims. *See* Pet.App. 3a, 7a, 8a; *see also* Exr. Ans. to App. Br. 47, 65, 73. This reference would not anticipate if the claim term "intermixture . . . from different sources" were construed to require more than one source of lipids, because walnuts constitute only one source of lipids. Further, if one or both of the claim elements "casings" and "dosage" were recognized not to be products of nature (discussed above), then claim 91 would be patent-eligible under § 101, as discussed above.

3. The Federal Circuit did not meaningfully review the Board's analysis of anticipation by the Mark reference

The Federal Circuit affirmed the Board's rejection of "claims 52, 61, 64, 65, 67-69, 73, 75, 77, 78, 80, 83, 90, 92-96, 98, 100, 129-131, 133, 135-137, 142 and 144 on the ground of anticipation by U.S. Patent No. 5,549,905 ["Mark"]." Pet.App. 3a, 10a, 14a. The court conclusorily set aside the "casing" and "dosage" limitations and failed to construe the claims with the required rigor. *See* Pet.App. 5a-6a (devoting a single paragraph to the issue). While the court affirmed a finding of anticipation of thirty claims, it specifically addressed only seven of these. The basis for finding the other twenty-three claims anticipated is not clear from the court's opinion. *See id.* 3a-6a.

4. Failure to meaningfully review anticipation of independent claim 91

The Federal Circuit did not meaningfully review the Board's analysis of anticipation of independent claim 91 and its dependent claims.

In its discussion of anticipation, the court did not address each of the four independent claims separately. The court stated that "claim 65 is the broadest claim" and "[o]ther claims add specificity of amounts or ratios, additional ingredients, sources of the lipids, and delivery methods." Pet.App. 2a-3a. Independent claim 91, at least, may be viewed as broader than claim 65, since claim 65 limits the ratio of omega-6 fatty acids to omega-3 fatty acids and claim 91 does not. Pet.App. 69a, 74a. Rather, claim 91 limits omega-6 fatty acids but not with respect to

omega-3 fatty acids, and it does not limit omega-3 fatty acids as a class. Pet.App. 74a.

Because each of claim 91 and claim 65 recite a material limitation that the other does not, any anticipation analysis of claim 65 does not apply to claim 91. Claim 91 stands rejected over only one of the cited references, "a serving of walnuts as reported in the Walnut Nutrient Analysis." Pet.App. 3a, 7a, 8a. The court's analysis referred to the omega-6/omega-3 ratio and the omega-6 less than 40 grams limitations, both of which occur in claim 65 but *neither* of which occur in claim 91. Pet.App. 8a, 69a, 74a. The court did *not* consider whether the reference disclosed the limitation "omega-6 fatty acids are greater than 20% by weight of the total lipids," which is present in independent claim 91 and its dependent claims. Pet.App. 8a-11a. The court therefore could not have fulfilled its obligation to meaningfully review the Board's finding of anticipation of claim 91 and its dependent claims.

That the Federal Circuit did not meaningfully review the rejections of claim 91 is further evidenced by the court's statement that "an omega-6 to omega-3 fatty acid ratio of 5:1" "is within the ratios in all of the '034 application claims." Pet.App. 4a. This statement suggests that the court did not appreciate that claim 91 is not limited with respect to "omega-6 to omega-3 fatty acid ratio." Pet.App. 74a.

5. Other instances of failure to meaningfully review

In the court's analysis under § 101, the court acknowledged petitioner's arguments that "the claimed limitations of 'dosage' and 'casings providing

controlled delivery' do not exist as natural products." Pet.App. 11a. Yet the court did not address or refer to these arguments in its § 101 analysis, and gave almost no analysis of these limitations in its anticipation analysis, as discussed above. *See* Pet.App. 11a-14a. A finding that these limitations establish that the claimed subject matter of *all* of the claims is not a product of nature would have defeated all of the § 101 rejections. This issue therefore should have received a reasoned analysis from the court. The Federal Circuit's glaring omission establishes that the court did not fulfill its obligation to meaningfully review the Board's findings of patent-ineligibility under § 101.

The court also failed to give meaningful review of numerous claims under §§ 101 and 102 because it provided few reasons to support its treatment of a large number of claims. *See* Pet.App. 3a-6a (treating anticipation of about thirty claims in three pages), 6a-10a (treating anticipation of over thirty claims over two references), 10a-14a (treating patent-ineligibility of about thirty claims).

A failure to provide meaningful review ultimately compromises judicial efficiency and fairness.

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted,

/s/

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August 28, 2018

ANNEX L:

Amicus Brief in Support of Petition for a Writ of Certiorari (case no. 18-277), October 5, 2018

No. 18-277

In the
Supreme Court
of the United States

URVASHI BHAGAT
Petitioner,

v.

ANDREI IANCU, DIRECTOR, UNITED STATES PATENT AND TRADEMARK OFFICE,
Respondent.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

Amicus Brief of Independent Inventors, Healthcare Professionals and Paul Gilbert Cole In Support of Petitioner Urvashi Bhagat

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Questions before This Court

This case raises fundamental issues concerning patent eligibility under 35 U. S. C. § 101, including:

> Is the standard of patentability expressed under *Funk Brothers*[1] moot or inapplicable in light of the 1952 Patent Act and the Supreme Court's decision of *Bilski v. Kappos*?[2] More specifically, does a "process" under § 101 require a "transformation," and is the standard of "invention" used in *Funk Brothers'* holding applicable to patent eligibility under 35 U. S. C. § 101?
>
> Also, did the Patent Trial and Appeal Board (PTAB) and Federal Circuit err by not construing the language of § 101 according to its ordinary, contemporary and common meaning?

In addition, *Amici Curiae* ask an additional question of this Court:

> Did the PTAB and Federal Circuit err by not considering the claims as a whole in both its § 101 and § 102 rejections.

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[1] *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948)
[2] *Bilski v. Kappos*, 561 U.S. 593 (2010)

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I. Identity and Interests of Amici Curiae

The Amici Curiae comprise U.S. Inventors, which is a nationally-recognized inventor association, joined by individual inventors, healthcare professionals specializing in the science of nutrition and businessmen. Amici Curiae include thousands of members. On behalf of all members, Amici Curiae promote policies that foster innovation, growth and a competitive marketplace for innovation. Amici Curiae members have a strong stake in the proper functioning of a predictable U.S. patent system. Amici Curiae's members also have a particularly strong interest in the development of appropriate standards for evaluating patent-eligibility under 35 U.S.C. § 101.

Paul Gilbert Cole is a practicing UK and European patent attorney, is a council member of the Chartered Institute of Patent Attorneys (CIPA), is a visiting professor in IP Law at Bournemouth University in the UK, and has been writing about and teaching patent law for some 40 years. Mr. Cole is concerned with the integrity of the legal system and the correctness of the consequential guidance that is given to patent examiners in the USPTO. It is his professional opinion that this Court should grant certiorari because the decision below does not conform with 35 U. S. C. § 101 or equivalent international standards of patent-eligibility.

Accordingly, Amici Curiae respectfully urge the Court to grant leave to file the present Brief, to grant Urvashi Bhagat's Petition and to reverse the decision below. Amici Curiae have no stake in the parties or in the outcome of the case beyond the deleterious effects of the instant Decision.[3]

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[3] No party's counsel authored this brief in whole or part; no party or party's counsel contributed money intended to fund preparing or

The names and affiliations of the Amici Curiae are set forth in the Appendix.

II. Reasons to Grant Certiorari

A. The Federal Circuit's Holding Violates Supreme Court Precedent Established in Bilski v. Kappos and Diamond v. Diehr.

The Supreme Court's decision in *Bilski v. Kappos,* 561 U.S. 593 (2010) set forth a number of important legal principles that the United States Patent and Trademark Office (USPTO) and the Federal Circuit have ignored for the last eight years. The first principle is the abrogation of the machine-or-transformation test as the sole test for patent eligibility under § 101. The second principle, related to the first, is this Court's recognition that there was no definition of the word "process" that requires a machine or transformation for patent eligibility under § 101. Yet it is the position of the USPTO and the Federal Circuit that some "transformation" is necessary for a process under § 101.

A correct holding reversing the decision below does not require a reversal of *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948). A reversal merely

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submitting the brief. No person other than the *Amici Curiae* or its counsel made a monetary contribution to its preparation or submission.

Amici Curiae provided notice to Petitioner Bhagat on September 21, 2018, of intent to file on behalf of Petitioner Bhagat, which is at least 10 days prior to the October 4, 2018, filing deadline as required under rule 37(2)(a). Amici Curiae also initially provided notice to Respondent on September 21st and again on September 22nd. Both Petitioner and Respondent have provided their consent.

requires recognition that the 1952 Patent Act substantively changed the statutory standard of patent-eligibility, and that proper claim construction principles discussed in *Bilski* render the holding of *Funk Brothers* moot or inapplicable. That is, there is no issue of *stare decisis* with regard to *Funk Brothers*. There is no decision or underlying principle for the Supreme Court to stand by because Congress, using its authority under Article I, Section 8, of the Constitution, changed the standard of patent-eligibility nearly seventy years ago.

In view of the change of statutory law since *Funk Brothers* was decided, it is the Amici's position that the decision below embodies an erroneous categorical rule that treats Petitioner's claims as falling outside the scope of § 101 by ignoring the ordinary, contemporary and common meaning of the statutory wording in 35 U. S. C. § 100 and 35 U. S. C. § 101.

Another reason to reverse the decision below is because, despite the rule set forth in *Diamond v. Diehr*[4] and repeated in *Alice Corp.*,[5] neither the USPTO nor Federal Circuit are yet convinced that claims under § 101 must be analyzed *as a whole*.

B. The Federal Circuit's Holding Is Detrimental to the Science of Nutrition

This case is an analog to *Bilski*. While *Bilski* addressed the patentability of business methods, this case addresses the patentability of nutrition science. However, unlike *Bilski*, which was directed to an extremely old process, *Bhagat* is directed to a new, specifically-tailored innovation to nutrition.

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[4] *Diamond v. Diehr*, 450 U.S. 175 (1981)

[5] *Alice Corp. PTY, Ltd v. CLS Bank Int'l*, 134 S.Ct. 2347 (2014)

The Federal Circuit does not apparently consider the science of nutrition important enough to warrant patentability consistent with the statutory language of § 101. Instead, the Federal Circuit has added an additional burden of some vague idea of "transformation" not found in the Patent Law and expressly disclaimed as a requirement to patentability in *Bilski*.

Innovation should be liberally encouraged in the science of nutrition as nutrition addresses a wide variety of preventable chronic diseases costing this country hundreds of billions of dollars every year.

While the science of lipids has barely been scratched, there are established studies indicating that inappropriate amounts/ratios of omega-6 and omega-3 oils in Western diets cause increased risks of cancer, cardiovascular disease, and inflammatory and autoimmune diseases. See, e.g., Simopoulos, Artemis, *The Importance of the Ratio of Omega-6/Omega-3 Essential Fatty Acids*, 56 Biomedicine & Pharmacotherapy 365-79 (2002). See also, William Harris et al., *Omega-6 Fatty Acids and Risk for Cardiovascular Disease*, 119 Journal of the American Heart Association 902-907 (2009).

Accordingly, the science of nutrition promises potential benefits for individual well-being, public well-being and national economics.

However, despite the known and unknown benefits of nutrition science, the Federal Circuit takes an unreasonable position that, without some nebulous standard of transformation, a new, useful and non-preemptive invention/discovery related to nutrition is not patent-eligible. By insisting on applying the machine-or-transformation test, the Federal Circuit created yet another categorical rule that "frustrate[s] the purposes of the patent law.'" *Bilski*, 561 U. S. at. 605 (citing *Chakrabarty*).

C. The Federal Circuit's Inability to Follow Supreme Court Precedent Is Detrimental to Innovation

The effects of the Federal Circuit's decision upon innovation are perilous. *Funk Brothers* may have been correctly decided under the patentability standards of 1948 when patent eligibility was determined by 35 U. S. C. § 31. However, today *Funk Brothers* is a relic that must be cast off. Decisions such as *Funk Brothers* were the impetus of the 1952 Patent Act, which was passed to rid the country of the stifling effects *Funk Brothers* and other such cases had on innovation.

By reverting to pre-1952 standards of patent eligibility while ignoring Supreme Court precedent, the Federal Circuit's jurisprudence threatens the stability and reliability of the patent system.

There is a quote found in the preface of *Nonobviosness – the Ultimate Condition of Patentability* (page v), a book that discusses patent-eligibility under § 101 as much as obviousness under § 103, that is particularly relevant.

> "[I]nventors and businessmen will be interested in the patent system only so long as they can reasonably understand the patent laws and rely on their stability. Indeed, when the government grant of a patent cannot reasonably be relied upon throughout the nation, then the patent system becomes a cruel hoax. An increase in trade secrecy and a decrease in innovation would be the result.
>
> The prevention of such a result has seldom been more important. There is no doubt that we must now encourage innovation. The reliability of patents has an important role to play in achieving that result. . . . . While a reliable patent system

> is not the whole answer, it is, nevertheless, a vitally important part of the answer." – Donald W. Banner, Commissioner of Patents and Trademarks (March 1979)

Since the *Bilski* decision, the U. S. patent system has dropped to No. 12 in patent protection and "joins a handful of other countries that are not thought of as being particularly intellectual property friendly."[6] The United States Chamber of Commerce's Global Innovation Policy Center reports that the U. S. presently "faces a growing level of uncertainty for innovators, particularly in relation to patent protection."[7] The Federal Circuit now uses the vague idea of "invention" to justify conclusory statements having no basis in preemption or the statutory language of § 101. See, e.g., *In re Villena*, Appeal No. 17-2069 (Fed. Cir. 2018). The Federal Circuit also advocates trade secrecy over patent protection. *SAP America v. Investpic* , 890 F.3d 1016, 1024 (Fed. Cir. 2018).

Innovation is waning, and even the head of the USPTO recognizes that the patent system is unstable.[8]

Amici assert that these detrimental effects are not caused by the lower courts following Supreme Court precedent. To the contrary, as will be discussed below, these detrimental effects are caused by the lower courts failing to follow statutory law, standard claim construction practices and this Court's precedent.

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[6] https://www.ipwatchdog.com/2018/02/08/u-s-patent-system-falls-12th-place-chamber-global-ip-index-2018/id=93494/

[7] http://www.theglobalipcenter.com/wp-content/uploads/2018/02/GIPC_IP_Index_2018.pdf at p. 157

[8] https://www.law360.com/articles/1032230/uspto-head-calls-for-new-path-to-restore-patent-stability

D. Other Issues

Regarding the anticipation rejection, *which does not extend to every claim*, it is of critical importance that this Court correct the Federal Circuit's violation of Petitioner's due process rights under § 706 of the Administrative Procedure Act (APA) that Congress mandated, and address the claims as a whole in its anticipation rejection as well as its patent-eligibility rejection. Because addressing the "claims as a whole" requirement under § 101 fully addresses the anticipation rejection, little additional effort is required to address the anticipation rejection.

III. Argument

E. Applicable Law

1. The Legislature, Not the Courts, Determines the Scope of Patent Eligibility

Article I, Section 8, of the United States Constitution states "***Congress*** shall have power . . . to promote the progress of science and useful arts" (emphasis added).

To this end, ***Congress*** enacted several different acts over time including the 1952 Patent Act.

Arguably, the two most significant changes of the 1952 Patent Act were: (1) to codify the holding of *Hotchkiss v. Greenwood*, 11 How. 250 (1850), so as to define patentability (not "invention") in terms of nonobviousness under 35 U. S. C. § 103; and (2) to replace the word "act" under then 35 U. S. C. § 31 with "process" under § 101 while defining the word "process" in § 100.

Section 101 states: "Whoever invents or discovers any new and useful ***process***, machine, manufacture, or composition of matter, or any new and useful improvement

thereof, may obtain a patent therefor . . . " (emphasis added). Relevant to the word "process," Congress defined the word in § 100 (b) as follows: "The term 'process' means process, art or method[.]"

While it is fully within the courts' powers to identify exceptions under § 101, it is not within the courts' powers to *de facto* rewrite a single word of the statutory patent laws, or to replace congressional intent with biases that the courts feel better suited to patent law. That is, *it is not within the constitutional powers of the courts to place a single additional burden on patentability that Congress did not sanction in its statutes*.

While courts may interpret particular words in view of congressional intent, the Supreme Court repeatedly declared that "[u]nless otherwise defined, 'words will be interpreted as taking their ordinary, contemporary, common meaning.'" *Bilski v. Kappos,* 561 U.S. at 603. "Our task . . . is the narrow one of determining what Congress meant by the words it used in the statute; once that is done, our powers are exhausted." *Diamond v. Chakrabaty*, 447 U. S. 303, 318 (1980).

2. The Federal Circuit's Decision Must Comply with the Statutory Requirements of the Administrative Procedure Act

Proceedings of the Board are governed by the APA, Title 5, §§ 551 et seq. *Allentown Mack Sales & Serv., Inc. v. NLRB*, 522 U.S. 359, 374 (1998). Section 706 of the APA recites:

> "To the extent necessary to decision and when presented, the reviewing court shall decide all relevant questions of law, *interpret constitutional and statutory provisions*, and determine the meaning or applicability of the terms of an agency action. The reviewing court shall—

> . . .
>
> (2) hold unlawful and set aside agency action, findings, and conclusions found to be—
>
> > (A) *arbitrary, capricious*, an abuse of discretion, or *otherwise not in accordance with law*" (emphasis added).

The Supreme Court's decision in *Dickenson v. Zurko*, 527 U. S. 150 (1999) stressed "the importance of not simply rubber-stamping agency fact-finding." *Id* at 162. "The APA requires meaningful review[.]" *Id.*

Under the APA, the Board is obligated not only to come to a sound decision, but to fully and particularly set out the bases upon which it reached that decision. *Sang-Su Lee*, 277 F.3d at 1342. The USPTO "must set forth its findings and the grounds thereof, as supported by the agency record[.]" *Id.* "Judicial review of a Board denying an application for patent is thus founded on the obligation of the agency to make the necessary findings and provide an administrative record showing the evidence on which the findings are based[.]" *Id.* Factual inquiries "must be based on objective evidence of record." *Id.* at 1343. "[R]eview of an administrative decision must be made on the grounds relied on by the agency." *Id.* at 1345. "If those grounds are inadequate or improper, the court is powerless to affirm the administrative action by substituting what it considers." *Id.* at 1345-46.

Petitioner Bhagat has every right to expect the USPTO and Federal Circuit to follow statute and established case law. It is a basic principle of fairness and due process that the government must follow the government's own rules.

F. The USPTO Failed to Address the Claims as a Whole Both under § 101 and § 102

The *Diamond v. Diehr* decision held that, in determining patent eligibility, "claims must be considered as a whole . . . ." *Diehr*, 450 U.S. at 188. *Mayo* v. *Prometheus* later clarified that, not only must claims be considered as a whole, but that all claim limitations must be considered individually and "as an ordered combination." *Mayo*, 132 S. Ct. at 1298. *Alice Corp*. repeated this rule. *Alice*, 134 S. Ct. at 2350, 2351, 2355 and 2359.

When addressing claims as a whole, words cannot be simply written out of a claim. "[T]he words of a claim are generally given their ordinary and customary meaning . . . . [Which is] the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Phillips v. AHW,* 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (citations and internal quotation marks omitted). "[T]he ordinary meaning of a claim term is its meaning to [an] ordinary artisan after reading the entire patent." *Id.* at 1321. (internal quotation marks omitted). "In some cases, the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words." *Id.* at 1314.

Turning to the instant decision, the PTAB and Federal Circuit both failed to address all claims limitations individually and as a whole, ordered combination. Exemplary claim 65 is reproduced below:

> 65. A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4: 1 or greater,

> contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein *at least one casing comprises an intermixture of lipids from different sources*, and wherein
>
> (1) omega-6 fatty acids are 4-75% by weight of total lipids and omega-3 fatty acids are 0.1-30% by weight of total lipids; or
>
> (2) omega-6 fatty acids are not more than 40 grams.

The PTAB expressly stated that it gave the limitation "*at least one casing comprises an intermixture of lipids from different sources*" zero weight because the word "casing" was not defined in the specification. Appx 5a-6a. While Petitioner's specification does state that "the compositions comprising the lipid formulation disclosed herein may be administered to an individual by any orally accepted form" (see Appx 6a), this at most means that the word "casing" can be broadly construed, *not completely ignored*.

The PTAB does not assert that the prior art or any natural phenomenon satisfies the limitation of *a single casing comprising an intermixture of lipids from different sources* – even under the broadest reasonable interpretation standard.

That is, rather than applying the "widely accepted" and "commonly understood" meaning of the word "casing," or even an unreasonably broad construction of the word, the PTAB and Federal Circuit wrote the word out of the claim entirely. This is inappropriate under § 101 and inappropriate under § 102.

For this reason alone, § 706 of the APA mandates that the PTAB's § 101 and § 102 rejections must be set aside.

IV. The Petitioner's Alleged "Product-by-Process" Claims Include a Process under § 101

A. There Are Two Types of Patent Eligibility Analysis under § 101

Assuming that an invention is new and useful, there is a distinct difference in patent eligibility analyses under § 101 that is often overlooked.

The first type of analysis is whether something is patent-eligible under § 101 by virtue of the definitions recited in § 100. An example of such an analysis is found in *In re Nuijten,* 500 F.3d 1346 (Fed. Cir. 2007) (holding that an electromagnetic carrier *per se* is not a process, machine, manufacture or composition of matter a defined by § 100). *In re Nuijten* reflects an example of a man-made invention that, as a categorical rule (not categorical exception), falls outside § 101.

The second type of analysis, which was addressed in *Alice Corp.*, is a determination of whether a claim constitutes an *exception* to § 101 by preempting a law of nature, natural phenomena or an "abstract idea." *Alice Corp.* commands courts to construe the abstract idea narrowly noting that the non-abstract "[poses] no comparable risk of pre-emption[.]" *Alice Corp.*, 573 S. Ct. at 2355.

The Federal Circuit's holding in the present case is not based on preemption, but instead is based upon the idea that, under a product-by-process construction (see Appx 29a), Petitioner's claims do not include a "process" under § 101.

B. The Claims Constitute a Process under § 101

Amici are aware that the USPTO and Federal Circuit agree that the present claims are directed to a product-by-process. Amici disagree with this product-by-process construction as does the Petitioner. However, even assuming that the present claims possibly may be construed as a product-by-process, the Federal Circuit's holding is still erroneous as Petitioner's claims would include a process under § 101.

As stated above, one of the major changes to the patent laws in the 1952 Patent Act was to replace the word "act" under then 35 U. S. C. § 31 with "process" under § 101 while defining the word "process" in § 100. As is also stated above, "[u]nless otherwise defined, 'words will be interpreted as taking their ordinary, contemporary, common meaning.'" *Bilski v. Kappos,* 561 U.S. 593, 603 (2010).

As was further recognized by the *Bilski* decision, there is no known meaning "of the definitional terms 'process, art or method' that would require these terms to be tied to a machine or to transform an article." *Id.*

Turning to the idea of the ordinary, contemporary and common meaning of the word "process" as related to patent law, *Black's Law Dictionary* (6th Ed. 1990) at p. 1205 defines "process" to mean: (1) an "art or method by which any particular result is produced;" (2) a "means or method employed to produce a certain result or effect;" and (3) "a definite combination of new or old elements, ingredients, operations, ways, or means to produce a new, improved or old result[.]"

Clearly, "a definite combination of new or old elements, ingredients, operations, ways, or means to produce a new, improved or old result" describes Petitioner's claims when

treated under a product-by-process construction. Appx. 5a-6a. A categorical rule differentiating Petitioner's claims from other forms of processes is improper. Such "categorical rule[s] denying patent protection for 'inventions in areas not contemplated by Congress . . . would frustrate the purposes of the patent law.'" *Bilski*, 561 U. S. at. 605 (citing *Chakrabarty*).

C. Bilski Holds That § 101 Does Not Require a Transformation, and Thus Funk Brothers Is Moot or at Least Inapplicable

As is stated by the Federal Circuit (Appx 12a, 14a):

> "The Board held that admixture with other natural products of known composition was *not shown or stated to change the nature of the compositions*, citing *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 131 (1948) ('The combination of species produces no new bacteria, no change in the six species of bacteria, and no enlargement of the range of their utility. . . . They serve the ends nature originally provided and act quite independently of any effort of the patentee.')
>
> .
> .
> .
>
> The Board found, and we agree, that the Applicant has not shown that the claimed mixtures are a '*transformation*' of the natural products, or that the claimed mixtures have properties not possessed by these products in nature" (emphasis added).

However, as stated above there is no known meaning "of the definitional terms 'process, art or method' that would require these terms to . . . transform an article." *Bilski*, 561 U. S. at. 603.

Thus, *Funk Brothers* is inapplicable due to the statutory changes of the 1952 Patent Act in light of the claim construction principles discussed in *Bilski*.

V. The *Funk Brothers* Holding Relied on "Invention," Which Congress Wrote Out of the Patent Law in 1952.

The 1952 Patent Act was enacted in response to the Supreme Court's anti-patent sentiment in the early 1900s. This anti-patent sentiment was reported by Karl Lutz (*The New 1952 Patent Statute*, 35: 3 Journal of the Patent Office Society, 155, 156-7 (1953)), who stated the 1952 Patent Act was enacted to remove "the recent apostasy" of the Supreme Court "from the benevolent policy of the Constitution." Indeed, the "apostasy" pre-1952 was so harsh that Justice Jackson criticized the Supreme Court's "strong passion" for striking patents down "so that the only patent that is valid is one which this Court has not been able to get its hands on." *Jungersen v. Ostby & Barton Co.*, 335 U. S. 560, 572 (1949).

The *Funk Brothers* decision was decided at the height of the pre-1952 "apostasy," and its use of the word "invention" was offensive to Congress.

Indeed, the *Funk Brothers* decision holds that "a product must be more than new and useful to be patented; it must also satisfy the requirements of *invention*" (emphasis added). *Funk Bros.*, 333 U. S. at 131. "[W]e think that aggregation of species *fell short of invention*

within the meaning of the patent statutes" (emphasis added) *Id.*

However, the term "invention" is meaningless. "Invention" lacks clarity. So much clarity that the Supreme Court admitted that "the word cannot be defined in such manner as to afford any substantial aid[.]" *McClain v. Ortmayer*, 141 U. S. 419, 427 (1891).

So much clarity that Congress and vast numbers of prominent attorneys and legal organizations conspired to rid the country of the word by codifying the 1952 Patent Act. See "*Efforts to Establish a Statutory Standard of Invention: Study of the Subcommittee of Patents, Trademarks, and Copyrights of the Committee on the Judiciary*" United States Senate; Eighty-fifth Congress, First Session Pursuant to Senate Resolution 55, Study No. 7 (published 1958) (hereinafter "the 1958 Study").

As stated on page 2 of the 1958 Study, Charles Kettering, who headed the National Patent Planning Commission, remarked that "[o]ne of the greatest technical weaknesses of the patent system . . . is the lack of a definitive yardstick as to what is invention."

On page 4 of the 1958 Study, the legendary Giles Rich remarked about the difficulty of overcoming the idea of invention concluding "[s]o long as invention is there they can say it isn't good enough to be an invention." Judge Rich's words are especially relevant today. Assuming that something is new, useful, falls within the subject matter of § 101 and doesn't preempt an abstract idea, what standard constitutes "good enough to be an invention?"

As Judge Rich further noted in *The Principles of Patentability* (17:2 Journal of the Patent Office Society, 75, 87-8 (1960)):

> "It has generally been stated to be the law that, in addition to being new and useful, an invention, to be patentable, must involve 'invention.' . . . Experienced patent lawyers, the Patent Office, and the courts understand 'What it means, only they never agree.'
>
> [There are] various meaningless phrases which have been used to express this essential mystery-something akin to a religious belief[.]
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> In the final analysis . . . [the] requirement for 'invention' was the plaything of the judges who, as they became initiated into its mysteries, delighted to devise and expound their own ideas of what it meant, some very lovely prose resulting" (internal citations omitted).

Judge Rich's biting commentary on the word "invention" is the reason "invention" was removed as a prerequisite to patentability in favor of nonobviousness.

Judge Rich, who was one of the primary drafters of the 1952 Patent Act, went on to say:

> "The Patent Act of 1952 expresses this [Section 103] prerequisite to patentability without actual reference to "invention" as a legal requirement. Nowhere in the entire act is there any reference to a requirement of "invention" and the drafters did this deliberately in an effort to free the law and lawyers from bondage to that old and meaningless term. The word "invention" is used only to refer to the thing invented. That is why the requirement of

> "invention" should be referred to, if at all, only with respect to that which is dead." *Id.* at 89.

See also, Rich, Giles, *The Vague Concept of "Invention" as Replaced by Section 103 of the 1952 Patent Act*, 46:12 Journal of the Patent Office Society, 855 (1964)).

The PTAB's and Federal Circuit's presumptive use of "transformation" and "invention" against Petitioner is not just an act of hubris, but a violation of statutory law, legislative intent and this Court's direction set out in *Bilski*.

VI. The Standard of "Transformation" Is Offensive to the Statutory Standard Created by Congress

As stated above, 35 U. S. C. § 101 recites: "Whoever invents or discovers any new and useful process, machine, ***manufacture***, or ***composition of matter***, or any new and useful improvement thereof, may obtain a patent therefor . . ." (emphasis added).

Noticeably missing from § 101 is the word "transformation" listed as a precondition to "obtain a patent therefor."

In addition, noticeably missing from the PTAB's and Federal Circuit's laments about Petitioner's claims is any discussion as to what standard of "transformation" is sufficient for patent-eligibility.

What is a sufficient "transformation?"

Take, for example, the world-changing invention of gunpowder, which is naught but a mixture of three naturally-found substances: charcoal, sulfur and potassium nitrate mixed in specific proportions. Each of these three

naturally-occurring components is not chemically changed when gunpowder is made. There is no "transformation" of naturally-occurring things as the Federal Circuit demands in order for a mixture to be patent eligible.

Assuming that gunpowder were invented today, would any justice on this Court deem the world-shaping invention of gunpowder as not patent-eligible under § 101 for lack of "transformation?"

Further, is carbon dissolved in iron sufficiently "transforming" of iron according to the Federal Circuit even though no chemical change is made?

Carbon aside, pure iron takes a variety of naturally-occurring allotropes. One naturally-occurring allotrope of iron (α) is ferromagnetic while another naturally-occurring allotrope of iron (ß) is not.

Certainly, turning ferromagnetic α-iron into non-ferromagnetic ß-iron sounds like a sufficient "transformation," but would most jurists consider turning α-iron into melted iron a sufficient transformation?

Note that turning α-iron into ß-iron requires only heating α-iron to the point where thermal agitation of iron atoms exceeds the oriented magnetic moment of unpaired electron spins. Heat the iron more and you have melted iron.

As with "invention," there is no standard of "transformation," and "transformation" isn't a requirement of patentability under § 101 anyway.

While there may be no "transformation" in the present claims that satisfies the USPTO's sensibilities, without doubt the presently claimed formulation qualifies as a "composition of matter" under § 101. The present claims recite a man-made mixture of different chemical entities from different sources in a defined proportion, and thus

clearly falls within the ordinary, contemporary and common meaning of a "composition of matter" under § 101.

Such a finding does not depend on the casing feature but is inherent and sufficiently defined by the mixture of substances alone. Substantive qualification, as opposed to mere appearance, is reinforced by the effects produced by fatty acids upon the human body as is discussed within the bounds of the present patent application as well as discussed in independent research including, but not limited to, the omega-3 / omega-6 articles cited above.

Further, if one does not merely ignore the "casing" limitation as did the PTAB and Federal Circuit, the claims also fall within the definition of a "manufacture" according to the ordinary, contemporary and common meaning of "manufacture" as is found in § 101.

Thus, it is most disturbing that the Federal Circuit abrogated both the "composition of matter" and "manufacture" language actually found in 35 U. S. C. § 101 in favor of a vague concept having no basis in § 101.

"Transformation" is an *ultra vires* creation of the Federal Circuit having no basis in the statutory framework Congress created in the Patent Law. This amounts to the Federal Circuit *de facto* re-writing the Patent Law (to omit two categories and add one of their own to § 101), which offends the doctrine of separation of powers.

VII. Conclusion

The claims clearly fall within the statutory framework of § 101, and a decision to the contrary sets precedent dangerous to the stability and reliability of the patent system. Further, read as a whole, Petitioner's claims are not anticipated. Accordingly, the Decision below should be reversed as well-settled principles of law.

Respectfully submitted,

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APPENDIX

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ANNEX M:

Supplemental Brief to Petition for a Writ of Certiorari (case no. 18-277), October 22, 2018, with the article, Bhagat U. "*Denying Patents on Applications of Discoveries Puts Public Health at Risk*

No. 18-277

In the Supreme Court of the United States

URVASHI BHAGAT,

Petitioner

v.

ANDREI IANCU, DIRECTOR, U.S. PATENT AND TRADEMARK OFFICE,

Respondent

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

SUPPLEMENTAL BRIEF

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Contents

SUPPLEMENTAL BRIEF

Petitioner submits this supplemental brief to present for the Court's consideration the article attached in the appendix hereto. Petitioner published this article after filing her petition for certiorari. The article is published online at https://www.ipwatchdog.com/2018/10/04/denying-patents-discoveries-puts-public-health-risk/id=101994/.

Respectfully submitted,

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October 22, 2018

APPENDIX A

Denying Patents on Applications of Discoveries Puts Public Health at Risk

By Urvashi Bhagat
October 4, 2018

In the 90s my mother was handed a death sentence at 61, a diagnosis of Progressive Supranuclear Palsy. It debilitates motor functions, like walking, speaking, swallowing, and progresses fast. Life expectancy after diagnosis is 7 years. Over the next few years she struggled to do simple tasks such as eating and passed away at 67. We were shocked as there was no incidence of neural disease in our family.

In hindsight I can trace mother's earliest symptoms, extremely sensitive teeth, breathing difficulty, and loss of balance to when she was in her 50s. The prevalent dietary advice for prevention of chronic health diseases in 80s and 90s was low-fat, low omega-6 fatty acids, and high monounsaturated fatty acids and primarily olive oil intake. Mother had adopted this advice because one of her brothers had died of heart disease at 48.

Troubled by mother's case, I began researching lipids (fats, certain vitamins and phytochemicals) in early 2000s. I was skilled in the field having majored in biology and chemistry. Scientific and mainstream literature then overwhelmingly taught reduction in omega-6 and increase in omega-3 to achieve omega-6 to omega-3 ratio of 2:1 or less. It

isn't just that they taught against excessive omega-6 but they taught extremely low omega-6 intake (e.g., less than 0.5% of calories or less than 1.11g/day for 2000 calories/day; see Landsin collaboration with US National Institutes of Health, Ann. N.Y. Acad. Sci. 2005;1055). Such teachings are still prevalent.

I made an important discovery in my own experiments: low dosage of omega-6 (e.g. less than 6 g/day for women) produced adverse health effects in live subjects, and when the dosage was increased at first the symptoms got worse, but after adjustment over few weeks at higher dosage of omega-6 (e.g. 11g/day for women) better health was achieved. Applying this principle, I was able to ameliorate and sometimes reverse adverse symptoms of chronic disease (e.g., high cholesterol, diabetes, ALS, ADHD, asthma) in live subjects at higher dosage of omega-6 (e.g., greater than 5% of calories).

In my findings, omega-6 was the most important fatty acid for health; its dosage was critical, and omega-6 to omega-3 ratios higher than 4:1 were found effective in general, particularly for high antioxidants and phytochemicals consumers. Current scientific research confirms my discoveries. It was now clear that my mother's neural disease was associated with extreme deficiency of certain lipids including omega-6 due to erroneous the teachings in 80s and 90s

In fact, most chronic diseases are associated with imbalanced lipid intake, and 117 million Americans suffer from these diseases. About $3 trillion annually is spent in US on treating those diseases. Despite the criticality of lipids, clear solutions are

not provided to the public. Rather there is confusion and misinformation.

Education about lipids alone is not enough, because healthy dosages of the various lipids vary for different members of the family and are hard to obtain. Lipid-rich foods such as oils and butters are unpredictable in lipid content. For example, omega-6 can be 6-80% in safflower oil and 2-20% in olive oil. Even olives from same tree vary seasonally in lipid content. Moreover, certain lipids are potent in micrograms, particularly from oils, because in concentrated state they are absorbed differently.

The problem has to be solved innovatively by providing pre-formulated tailored lipid dosages to the public. This innovation will not only reduce the disease burden and healthcare costs but will also make further contributions by affecting downstream actions of others. So, I founded Asha Nutrition Sciences in 2008 with the main product offering of packaged tailored lipid dosages using different lipid sources to control the lipid content, and filed for patents, because without patents we could not fund the effort. Patents are the lifeblood of innovation; without a patent there is simply no way to obtain the funding necessary to implement this complex innovation.

To be clear there is no statutory prohibition on nutrition patents. The US statute of "patent eligibility" 35 USC § 101 simply states, "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions

and requirements of this title."

However, in practice the patent system severally [sic, *severely*] restricts nutrition patents, such as to my innovation.

Because of such patent practice, lipid delivery fundamental to public health have not materially advanced since the invention of food oils approximately 6000 years ago. Periodically, certain fatty acids (e.g., omega-3) or oils or low-fat teachings have been hailed, only to reverse a few years later. To date random oils are randomly added to foods; no guidance is given that different batches of the oils can have significantly different lipid composition and that minor lipids components present in oils can be potent. Oil making has advanced but delivery of oil for ingestion by subjects is still archaic.

Instead, the patent approval process favors patent grant to drugs, devices, and structurally altered molecules. Under the circumstances it is to be expected that prevention would not receive attention from medical practitioners. Additionally, structurally altered molecules (e.g. hydrogenated fats) favored by the patent practice have previously caused worldwide diseases for over 100 years. Because the patent practice refuses to grant patents that solve the problem head-on, divergent mini-solutions are developed, which make things worse.

After nine years of costly legal proceedings the United States Patent Office denied the patent by misapplying the law. The Court of Appeals for the Federal Circuit rubberstamped the Patent Office and issued an evasive non-precedential opinion—

meaning this ruling does not apply to other cases. The case is now appealed to the Supreme Court of the United States.

While I am frustrated with the Patent Office, and the Federal Circuit, the real problem is that the U.S. Supreme Court has given conflicting guidance on patent eligibility despite the clear and unambiguous terms of § 101. Thus, unless and until Congress steps in – and they should – innovators like me have no choice but to throw myself on the mercy of the Supreme Court and ask them to consider the magnitude of the harm their rulings have created.

During the nine years the patent application has been pending, 13.6 million Americans have died of associated chronic diseases. While the Government denies any responsibility, I beg to differ. Advancement in the art must be the overriding constitutional standard, and where there would be a positive effect on society a patent must not be denied. Denying patents on such significant advances, which will not take place without patent protection, goes against everything the patent system is supposed to promote.

I trust that the Supreme Court will reverse the prior decisions and restore confidence that our legal system does indeed work!

ANNEX N:

Petition for a Writ of Mandamus to the Supreme Court of the Unites States, March 30, 2019 (case no. 18-1274)

APPENDIX A	Federal Circuit Opinion March 16, 2018, **omitted** since it is attached here as Annex H
APPENDIX B	Patent Trial and Appeal Board Decision on Petition (Denying Review), August 16, 2016, **omitted**
APPENDIX C	Patent Trial and Appeal Board Decision on Request for Rehearing (Denying Rehearing), June 21, 2016, **omitted**
APPENDIX D	Patent Trial and Appeal Board Decision on Appeal, April 15, 2016, **omitted** since it is attached here as Annex G
APPENDIX E	Federal Circuit Order (Denying Rehearing), June 1, 2018, **omitted**
APPENDIX F	Statutes, **omitted**
APPENDIX G	Claims at Issue Below, **omitted** since those are attached here at the end of Annex A
APPENDIX H.	Bhagat U. *Denying Patents on Applications of Discoveries Puts Public Health at Risk,* **omitted** since it is attached here as Annex M
APPENDIX I.	Bhagat U. Das UN. *Potential role of dietary lipids in the prophylaxis of some clinical conditions,* **omitted** since it is attached here as Annex Y

No. _____

In the

Supreme Court of the United States

IN RE URVASHI BHAGAT

Petitioner

On Petition for a Writ of Mandamus to the United States Court of Appeals for the Federal Circuit and United States Patent and Trademark Office

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Petition for Writ of Mandamus

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QUESTIONS PRESENTED

Congress set the test for patent eligibility under Title 35 U.S.C. §101 of the 1952 Patent Act as: "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." The Supreme Court's longstanding and highly-respected decision of *Graham v. John Deere*, 383 U.S. 1, 12-13 (1966) recognized it was Congress' intent to replace "invention" with non-obviousness as the test for patentability given the term "invention" is meaningless. The Court also held in *Bilski v. Kappos,* 561 U.S. 593 (2010) the Federal Circuit's "Machine or Transformation" test was flawed stating there was no definition of "process" under 35 U.S.C. §100(b) requiring "transformation" for a claim to be patent eligible. Given the clear statutory language of §101 and this Court's precedent, the questions are:

1. Whether the United States Patent and Trademark Office (USPTO) abused its discretion by refusing to allow claims that passed every single requirement of Title 35 of the United States Code by insisting these perfectly patent-eligible claims must pass the extra-statutory requirements of "transformation" and "invention."

2. Whether the United States Court of Appeals for the Federal Circuit abused its discretion under the statutory requirements set forth by the Administrative Procedure Act (APA), Title 5 U.S.C. §706 by refusing to set aside a USPTO decision that is arbitrary, capricious, and not in accordance with statutory law or this Court's precedent.

CORPORATE DISCLOSURE STATEMENT

Asha Nutrition Sciences, Inc. owns 100% of U.S. Patent Application No. 12/426,034, the patent application at issue. Asha Nutrition Sciences, Inc. has no parent company, and no publicly held corporation owns 10% or more of its stock. Petitioner Urvashi Bhagat is the applicant in the '034 application and is president of Asha Nutrition Sciences, Inc.

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The opinion of the Court of Appeals for the Federal Circuit (Pet.App. 1a-13a) is reported at 726 Fed. Appx. 772. The opinion of the Patent Trial and Appeal Board (Pet.App. 21a-58a) is unreported.

JURISDICTION

The Court of Appeals for the Federal Circuit issued its decision on March 16, 2018. A combined petition for panel rehearing and rehearing *en banc* was denied on June 1, 2018. Pet.App. 59a-60a. This Court has jurisdiction to grant a writ of Mandamus. *See* 28 U.S.C. § 1651(a).

STATUTORY PROVISIONS INVOLVED

Title 35 U.S.C. §101:

> "Inventions patentable. Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."[1]

Title 5 U.S.C. § 702:

> "A person suffering legal wrong because of agency action, or adversely affected or aggrieved by agency action within the meaning of a relevant statute, is entitled to

[1] Congress codified the language of §101 in the 1952 Patent Act that has not changed since.

> judicial review thereof. An action in a court of the United States seeking relief other than money damages and stating a claim that an agency or an officer or employee thereof acted or failed to act in an official capacity or under color of legal authority shall not be dismissed nor relief therein be denied on the ground that it is against the United States..."

Title 5 U.S.C. § 706:

> To the extent necessary to decision and when presented, the reviewing court shall decide all relevant questions of law, interpret constitutional and statutory provisions, and determine the meaning or applicability of the terms of an agency action. The reviewing court shall—
>
> (1) compel agency action unlawfully withheld or unreasonably delayed; and
>
> (2) hold unlawful and set aside agency action, findings, and conclusions found to be—
>
> (A) arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law;
>
> (B) contrary to constitutional right, power, privilege, or immunity;
>
> (C) in excess of statutory jurisdiction, authority, or limitations, or short of statutory right;
>
> (D) without observance of procedure required by law;

> (E) unsupported by substantial evidence in a case subject to sections 556 and 557 of this title or otherwise reviewed on the record of an agency hearing provided by statute; or
>
> (F) unwarranted by the facts to the extent that the facts are subject to trial de novo by the reviewing court.
>
> In making the foregoing determinations, the court shall review the whole record or those parts of it cited by a party, and due account shall be taken of the rule of prejudicial error.

STATEMENT OF THE CASE

Exceptional circumstances in this case warrant the exercise of this Court's discretionary powers to mandate the case back to the Federal Circuit. In an extreme case of abuse of discretion USPTO rejected *55 claims* (Pet.App. 63a-84a) under 35 USC §101 and §102 in the examination and appeal of US Patent Application 12/426,034 by excising *many* limitations from *many* claims, because otherwise no rejections could be maintained. Petitioner appealed the eligibility and anticipation rejections to the Federal Circuit, however the Federal Circuit issued an *incoherent* opinion rubber-stamping USPTO, failing to answer Petitioner's arguments, failing to review several independent and dependent claims, and failing to meet the statutory requirements set forth by the Administrative Procedure Act (APA), Title 5 U.S.C. § 706 by refusing to set aside the USPTO decision that is arbitrary, capricious, and is contrary to statutory law and this Court's precedent.

Mandamus is warranted *at least* on the basis of sole rejection Claims 102, 107, and 119 under 35 USC §101.

A. Action At USPTO

Petitioner filed the present application on April 17, 2009. Independent claim 65 is reproduced below. The four independent claims 65, 91, 129, and 130 and all dependent claims are reproduced in the Appendix. Pet.App. 63a-84a.

> 65. A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4: 1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids from different sources, and wherein
> (1) omega-6 fatty acids are 4-75% by weight of total lipids and omega-3 fatty acids are 0.1-30% by weight of total lipids; or
> (2) omega-6 fatty acids are not more than 40 grams.

The claimed features are poorly understood and prior art overwhelming incorrectly teaches the opposite (extremely low intake of omega-6, increased relative intake of omega-3, and use of other lipids to suppress omega-6 actions), leading to catastrophic public suffering because improper intake of lipids including omega-6 is associated with most chronic

diseases and monumental social and national burden (Pet.App. 85a-133a). Poorly understood factors are evidenced by the fact that no reference could be found that *necessarily* functions and teaches as claimed, though subject matter is directed to critical public health need. This is evident from the type of prior art USPTO had to rely upon to reject the claims under §101 and §102, since §103 rejections could not be sustained because of overwhelming opposite teachings in prior art.

To reject the claims under §102 USPTO had to rely upon Mark patent (US5549905A), which does *not* necessarily function as "at least one casing comprises an intermixture of lipids from different sources", or "omega-6 to omega-3 ratio is 4:1 or greater [in total lipids]", or wherein omega-6/omega-3 fatty acid concentrations are taught relative to "total lipids", or wherein dosage of "omega-6 fatty acids are [is] not more than 40 grams." Mark teaches "*a* lipid source" in claims 1, 9, and 15; "omega-6 (n-6) to omega-3 (n-3) ratio of [up to] 6:1" in *triglycerides* in col. 4—not total lipids—with omega-6 to omega-3 ratio of 1:4 to 1:6 in col. 2; and maximum concentration of linoleic acid—not total omega-6 fatty acids—of "12.2% by weight of fatty acids" in col. 4. It is the basic requirement of §102 rejection that the cited art *must necessarily* function as and enable the claimed invention, which Mark does not, Mark is also inoperable due to missing parts and contradictions in the disclosure. *Perricone v. Medicis Pharm. Corp.* 432 F.3d 1368, 1376 (Fed. Cir. 2005).

Further, because even by improper standards USPTO could not allege Mark anticipates present

Claim 82 (dependent on Claim 65) reciting "wherein the omega-6 to omega-3 ratio is greater than 6:1… or… at least 9:1" (Pet.App. 67a) or present Claim 91 (and claims dependent on 91) reciting "wherein the omega-6 fatty acids are greater than 20% by weight of the total lipids" (Pet.App. 68a-69a), nutrient profile of a batch of walnuts or olives, *each individually,* was relied upon to allege anticipation of Claims 82 and 91 under §102, by excising "dosage", "casing(s)", and "providing controlled delivery of the formulation to a subject," from the claims and constructing, "at least one casing comprises intermixture of lipids from different sources" as product-by-process limitation (Pet.App. 46a-58a), though Specification is clear the intermixture is employed to control lipid content of the formulation (Fed.Cir.App. Appx62).

Thus, the antics USPTO had to rely upon to allege anticipation itself indicates lack of anticipation, because without a doubt, if public is in possession of the nutritional invention *critical* to public health then *many nutritional guidelines precisely teaching* the claimed subject matter should be available, not just ambiguous and unenabled Mark and far from the claimed inventions individual nuts in measures ranging from tablespoon to cups comprising unpredictable lipid amounts.

Thus, USPTO applied §103-type rejections under §102 because §103 rejections could not be sustained. **However, even by improper standards, USPTO could not reject Claims 102 and 107 (dependent on Claim 65) and Claim 119 (dependent on Claim 91) under §102, which were then improperly rejected under**

§101, even after admitting no product of nature meets the combination of ratios of fatty acids recited in these claims[2].

Patent and Trial and Appeal Board at USPTO issued its decision on April 16, 2016, reconstructing and optimizing each of Mark, walnuts, and olives in hindsight to allege inherency of all claimed elements and constructed "intermixture of lipids from different sources" as product-by-process limitation and distorted and disregarded expert testimony to maintain §102 rejection of Claims 52, 61, 64, 65, 67-69, 73-75, 77, 78, 80, 83, 90, 92-96, 98, 100, 129-131, 133-137, 142, and 144 over Mark, of Claims 52, 61, 64, 65, 67–69, 73–75, 77, 78, 80, 83, 90–101, 116–118, 120–122, 128–140, and 141–145 over walnuts, and of Claims 52, 61, 64, 65, 67–69, 73–75, 77, 78, 80, 82, 83, 90, 92–94, 96–98, 100, 129–131, 133, 137, 142, and 144 over olives (Pet.App. 34a-58a).

Further, the Board maintained rejection of *all 55 claims* under §101 as products of nature drawn to alleged products of nature walnut oil or olive oil, *each individually*. **Board maintained "intermixture of lipids from different sources" is a product-by-process limitation alleging Petitioner has not provided evidence of *transformation* from a single source.** Furthermore, the Board ***excised*** "dosage" and "casings providing controlled delivery of the formulation to a subject" and "at least one casing comprises an intermixture…" from the claims (Pet.App. 27a-29a). The Board relied upon *Funk Bros. Seed Co. v. Kalo Inoculant Co.,* 333 U.S. 127,

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[2] Fed.Cir.App. Appx7436

129 (1948) and *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2118 (2013) (DNA analysis rather than cDNA analysis) in maintaining §101 rejection of claims 52, 61, 64, 65, 67–69, 73–75, 77, 78, 80, 82, 83, 90–102, 107, 116–122, 124, and 128–145 (Pet.App. 26a-34a, 58a).

B. Action At The Federal Circuit

Petitioner appealed *pro se* to the Federal Circuit.

Petitioner asserted the Board's claim construction fails to meet the basic principle of claim interpretation and is legally incorrect as it excises terms, disregards context and substantial intrinsic evidence including skilled persons' testimony and provided correct claim construction. (App.Br. 36-37, 39-49).

Under §102, Petitioner asserted the Board had reconstructed and optimized Mark in hindsight to allege anticipation assuming things Mark neither disclosed nor enabled, Mark was inoperable due to gaps (e.g., missing fatty acids in table in col. 4, contradictions in ratios in col. 2 verses 4, and contradictions within table in col. 6) and confounding lexicography (describing lipid sources as "lipid"), product-by-process construction as being drawn to any single source like olives/walnuts was disclaimed during prosecution, and Board had reconstructed all of the references in hindsight using Petitioner's own disclosure against the Petitioner and none of the references necessarily function as claimed. (App.Br. 37-38, 59-78).

Petitioner further asserted that it is an unjustifiable legal error to disregard the limitation "at least one casing comprises an intermixture of lipids from different sources" and it is a product limitation in a product [formulation] claim, which is devoid of product-by-process wording. (Rep.Br. 4-7).

With respect to §101 Petitioner asserted,

The very purpose of the present inventions comprising process and composition of matter (dosages, casings, controlling delivery, intermixtures) is to solve the problem of deficiency, excess, or unpredictability in products of nature. (App.Br. 50-52).

"[a]ppealed claims are neither drawn to a variety of fruit, nut, vegetable, including by-process, nor to isolated omega-6, omega-3, or any other lipid, additionally, the claims include transformative processes (§100(b)): dosage, casings providing controlled delivery, and intermixtures with implied unexpected differences over a "single" source. **There is NO PREEMPTION of any product of nature, and each of the features, formulations, dosages, casings providing controlled delivery of the formulation to a subject, intermixtures of lipids from different sources, and defined lipid content embodies *'a nonnaturally occurring manufacture or composition of matter—a product of human ingenuity 'having a distinctive name, character [and] use'*."** (App.Br. 53).

Petitioner also asserted that due to the abuse of discretion by USPTO the Federal Circuit must reverse USPTO's decision. (App.Br. 38, 80).

The Federal Circuit issued its opinion on March 16, 2018, sweepingly rubber-stamping the Board's decision without a providing any meaningful review. **A writ of mandamus is warranted because the right to issuance of the writ is clear and indisputable at least based upon claims 102, 107, and 119 (Pet.App. 11a-12a, 71a, 73a), solely rejected under §101 where USPTO admitted the claimed compositions are not known to occur in nature[3], there is no other means to attain adequate relief, and there is judicial usurpation of power and clear abuse of discretion.**

[3] Fed.Cir.App. Appx7436

STANDARD OF REVIEW

The Supreme Court has the power to "issue all writs necessary or appropriate in aid of their respective jurisdictions and agreeable to the usages and principles of law." 28 U.S.C. § 1651(a). A writ of mandamus is warranted when a party establishes that (1) the "right to issuance of the writ is clear and indisputable"; (2) the party has "no other adequate means to attain the relief" sought; and (3) "the writ is appropriate under the circumstances." *Cheney v. U.S. District Court*, 542 U.S. 367, 380-81 (2004) (internal quotation marks omitted).

A writ is appropriate in matters where the applicant can demonstrate a "judicial usurpation of power" or a clear abuse of discretion. See id. at 380 (citations and quotations omitted); see also Roche v. Evaporated Milk Ass'n, 319 U.S. 21, 26 (1943) ("The traditional use of the writ in aid of appellate jurisdiction both at common law and in the federal courts has been to confine an inferior court to a lawful exercise of its prescribed jurisdiction or to compel it to exercise its authority when it is its duty to do so.").

REASONS TO GRANT MANDAMUS

I. The Astounding Breadth of The Federal Circuit's Improprieties Evidences Clear Abuse of Discretion

The Federal Circuit *sweepingly* regurgitated USPTO decision without providing meaningful

review required by APA, Title 5 U.S.C. § 706, and issued an incoherent opinion (e.g., acknowledged prosecution disclaimer to "single source" but then disregarded it in affirming anticipation by "single source" without explanation, discussed below) at the expense of *pro se*. This Court has "stressed the importance of not simply rubber-stamping agency fact finding." *Dickinson v. Zurko*, 527 U.S. 150, 162-63 (1999).

A. Failed to Meaningfully Review Claim Construction

There is no principled claim construction in the opinion though Federal Circuit standard is to review "Board's claim constructions de novo." *Microsoft Corp. v. Proxyconn, Inc.*, 789 F.3d 1292, 1297 (Fed. Cir. 2015) (citing *Teva Pharms. USA Inc. v. Sandoz Inc*, 135 S. Ct. 831, 841-42 (2015)). The opinion affirmed Board's excision of "dosage", "casings providing controlled delivery of the formulation to a subject", and "at least one casing comprises an intermixture" from the claims (Pet.App 5a-6a) despite the precedent, "A claim construction that gives meaning to all the terms of the claim is preferred over one that does not." *Merck & Co., Inc. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir. 2005); and *Warner-Jenkinson Co., Inc. v. Hilton Davis Chemical Co.*, 520 U.S. 17, 29 (1997). The USPTO and Federal Circuit fabricated "the specification states that these claim elements are not limiting" (Pet.App. 6a). Specification actually provides, "It is intended that the following claims define the scope of the disclosure and that methods and structures within the Scope of these claims and

their equivalents be covered thereby." (Fed.Cir.App. Appx97, emphasis added). The Federal Circuit improperly alleged "[Specification] does not describe any assertedly novel characteristics of these components or their formulations" (Pet.App. 6a); Rather Specification gives *six* tables and *twenty* examples emphasizing the importance of "dosage" and steady dosage (Fed.Cir.App. Appx66-67, Appx71-77, Appx82-97).

The Federal Circuit evaded to answer Petitioner's submissions rebutting the *crux* of USPTO rejections—the product-by-process construction of the limitation "intermixture of lipids from different sources" and the claims as a whole (App.Br. 15, 21-22, 27, 36-37, 45-46, 52-53, 64, 71-73; Rep.Br. 4-7). The opinion acknowledged, "Applicant states that the Board erroneously ignored a prosecution disclaimer of all compositions containing products from single sources like olives and walnuts" (Pet.App. 8a) "thus avoiding not only anticipation, but also Section 101" (Pet.App. 10a), but then disregarded the *undisputed fact* and affirmed the alleged anticipation by olives or walnuts (Pet.App. 9a-10a) and ineligibility over single source oil (Pet.App. 13a) without explanation.

Further, *many* limitations from *many* claims were excised to allege ineligibility and unpatentability (App.Br. 12, 16-17, 34, 58-59, 67-68, 76-78). As USPTO admitted, the *combination* of ratios of fatty acids present in Claims 102, 107, and 119 is not known to occur in nature. The Petitioner asserted walnuts, olives, or their oils do not meet the forceful limitation present in these claims "ratio of monounsaturated fatty acids to polyunsaturated

fatty acids is in the range of 1:1 to 3:1" (App.Br. 34, 58-59, 77-78). The opinion makes *no mention* of this and incoherently states,

> "Claim 102 recites specific ratios of polyunsaturated, monounsaturated, and saturated fatty acids. Claims 107 and 119 present the fatty acid content recited in claims 98 and 91, respectively, in Tables in the specification. The Board observed that the servings of olive oil and walnut oil shown in the references contain omega-6 and omega-3 fatty acids in amounts within the Applicant's claimed ranges. Thus the Board held that the 'intermixture of lipids from different sources' does not distinguish the claims from natural products because the Applicant 'has not provided adequate evidence that an oil from different sources would necessarily have a composition that is different from one from the same source, nor that a different source would necessarily impart characteristics to the formulation which were absent when a single source was used.' Board Op. at *8." (Pet.App. 12a).

Thus, the Federal Circuit disregarded the arguments and glaring evidence present <u>*on the face*</u> of the cited references that the "ratio of monounsaturated fatty acids to polyunsaturated fatty acids is in the range of 1:1 to 3:1," expressly recited in Claim 102 (Pet.App. 71a) is <u>*different*</u> from the cited references[4].

B. <u>Required "Transformation" Under §101 Contrary to Bilski</u>

[4] Fed.Cir.App. Appx6969-6970, Appx6984-6985

The Federal Circuit acknowledged Petitioner's assertions that single source was disclaimed during prosecution, the properties of the claimed formulations from different lipid sources are different from the properties of single source natural products, the claimed limitations of "dosage" and "casings providing controlled delivery" do not exist as natural products and nature cannot provide a controlled delivery or dosage because lipid profiles in nature are unpredictable and that walnut oil and olive oil are not "natural products" (Pet.App. 10a-11a), but then inexplicably went ahead and disregarded the assertions anyway, affirming the §101 rejection stating,

> "The Board found, and we agree, that the Applicant has not shown that the claimed mixtures are a "transformation" of the natural products, or that the claimed mixtures have properties not possessed by these products in nature." (Pet.App. 13a).

Thus, the Federal Circuit decided "transformation" is a necessary standard for eligibility under §101 contrary to this Court's ruling in *Bilski*[5], moreover it required "transformation" over *non-natural products* (oils) containing *extraneous features* (capacity measures like tablespoons).

C. Acknowledged Prosecution Disclaimer of Single Source Like Olives or Walnuts, Then Disregarded it And Affirmed §102 Rejection Over Olives/Walnuts

[5] This case is not related to the preemption-based exceptions to patent-eligibility outlined in the *Alice/Mayo* test.

Contrary to *In re Zletz,* 893 F.2d 319, 321-322 (Fed. Cir. 1989) despite acknowledging "prosecution disclaimer of…olives and walnuts" (Pet.App. 8a), the Federal Circuit overlooked this undisputed fact in ruling anticipation by olives/walnuts (Pet.App. 9a-10a); and contrary to a large body of its own case law Federal Circuit disregarded that walnuts/olives are indisputably non-anticipatory because neither discloses and necessarily function as "at least one casing comprises an intermixture of lipids from different sources." *Perricone* 1376.

D. Failed to Meaningfully Review §102 Rejections under Mark

The Federal Circuit adopted Boards' reconstruction and optimization of Mark. Despite Petitioner's pleas (App.Br. 30-32, 60), the Federal Circuit failed to determine "ordinary meaning" and "scope" of Mark *de novo* as a matter of law in temporal context (*Teva* 837); failing to read Mark's "lipid" means lipid source that comprise non-lipids (col. 5.ll.59-62) and "source" means source of nutrients (col. 4.ll.19-20). Further, the opinion *glaringly misquotes* Mark. For example, the opinion states, "Mark describes a nutritional composition [] containing omega-6 and omega-3 fatty acids in a ratio of 'approximately 4:1 to 6:1.' Mark, col. 2.ll.32–38 (Pet.App. 3a). However, that is the *complete opposite* of Mark's disclosure in col. 2.ll.32–38, where Mark discloses "omega-**3** to omega-**6** fatty acid ratio of approximately 4:1 to 6:1;" [6] the opinion also

[6] Fed.Cir.App. Appx8102

misrepresents Mark's disclosure in col. 4. ll.21–23 (Pet.App. 3a), where the correct disclosure is "The lipid profile containing such *long chain triglycerides* is designed to have a polyunsaturated fatty acid omega-6 (n-6) to omega-3 (n-3) ratio of approximately 4:1 to 6:1."[7] The opinion further *misrepresents*, "Mark states that the omega-6 fatty acid 'is present in a range of approximately 4–6% of the total calories' of the pediatric composition, and the omega-3 fatty acid 'is preferably present in the range of approximately 0.8–1.2% of the total calories.' *Id.* col. 4.ll.27–31." (Pet.App. 3a-4a). However, Mark discloses "the *source* of omega-6 fatty acids is present in a range of approximately 4-6% of the total calories. The omega-3 fatty acid *source* is preferably present in the range of approximately 0.8-1.2% of the total calories" (col.4.ll.27-31) and "source" means oils and the like (col. 4.ll.19-20)[8], which contain other lipids and non-lipids not just omega-6/omega-3. (Emphasis added to Mark's disclosures.) These misrepresentations disregarded Petitioner's repeated rebuttals of the allegations in the briefs (App.Br. 23-26, 30-33, 59-66; Rep.Br. 17-21). The points are critical because they establish ambiguity, non-enablement, and inoperability of Mark's disclosure—which the opinion fails to answer—and therefore non-anticipation. (App.Br. 65-66, 67; Rep.Br. 23-26).

The opinion *avoided* to answer Petitioners repeated assertions that there is no recitation of "at least one casing comprises an intermixture of lipids from different sources" in Mark, and it claims "*a* lipid

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[7] Fed.Cir.App. Appx8103
[8] Fed.Cir.App. Appx8103

source" in claims 1, 9, and 15 (App.Br. 25, 64; Rep.Br. 4-7, 22-23).

E. Failed to Cite Law Based Upon Which The Case is Decided

Under §101 rejections there is no mention of requirements of §101, under §102 rejections there is no mention of the authorities relied upon in deciding the case. Only passing mention is of *Funk Bros.* in review of dependent Claim 128(1) under §101 and of *In re Oetiker* in review of dependent claims under §102. (Pet.App 9a, 10a).

F. Failed to Review Many Claims Including Independent Claims

For example, independent Claims 129 and 130, and dependent claims 68, 69, 73, 96, 98, 100, 142, and 144 under Mark (Pet.App. 3a-6a) were left unexamined.

G. Failed to Acknowledge Eleven Expert Testimonies Repeatedly Cited in Petitioner's Briefs

Contrary to its own precedent, *In re Alton*, 76 F.3d 1168, 1175-77 (Fed.Cir. 1996), the Federal circuit made no mention of *eleven* testimonies from skilled persons[9] testifying, claimed subject matter is poorly understood, claimed inventions have great potential to meet the critical unmet public health

[9] Fed.Cir.App. Appx3849-3869, Appx5702-5705, Appx6479-6529, Appx7228-7245, Appx7318-7327, and Appx7356

need and protect and enhance public health, nature is unpredictable in lipid content to provide dosage of lipids, intermixture of lipids from different sources necessarily has different chemical properties than a natural lipid source, Mark is ambiguous, unenabled, and inoperable, and olives/walnuts do not teach dosage of omega-6 and omega-3, they teach random use of olives and walnuts, despite Petitioner's repeated pointing to the testimonies. App.Br 43-45, 51, 62-66, 70, 74-75; Rep.Br 15-16, 21-24.

The above demonstrate **a clear and sweeping case of abuse of discretion** where the Federal Circuit failed to provide a meaningful (or any) review as required by APA. *Cheney 380* and *Roche 26*. The Federal Circuit mindlessly disposed the case demonstrating undue bias at the expense of *pro se* and compromised the credibility of the judiciary.

The following discussion focuses on §101 rejections, particularly claims 102, 107, and 119 solely rejected under §101, demonstrating quick review process and clear right to mandamus.

II. Judicial Usurpation Of Power

A. The Legislature Not Courts Determine the Scope of Patentability

The recent decision *Henry Schein, Inc. v. Archer and White Sales, Inc.*, Case No. 2017-1272 (January 2019) holds the courts "are not at liberty to rewrite the [Federal Arbitration Act] statute passed by Congress and signed by the President." *Schein*, slip op. p.1. The *Schein* decision (slip op. p.2) also holds

the courts "may not engraft our own exceptions onto the statutory text" citing *Exxon Mobil Corp.* v. *Allapattah Services, Inc.*, 545 U.S. 546, 556–557 (2005). "We must interpret the Act as written." *Schein* slip op. p.5. It is clear this Court recognizes it is not acceptable to alter the text of a statute that "is inconsistent with the statutory text and with our precedent." *Schein* slip op. p.8.

> Article I, Section 8, of the United States Constitution states "***Congress*** shall have power… to promote the progress of science and useful arts" (emphasis added).
>
> To this end, ***Congress*** enacted several different acts over time including the 1952 Patent Act.
>
> Section 101 of the 1952 Patent Act states: "Whoever invents or discovers any new and useful ***process***, machine, **manufacture**, or **composition of matter**, or any new and useful improvement thereof, may obtain a patent therefor…" (emphasis added).
>
> ***Congress*** defined "process" in §100(b) as follows: "The term 'process' means process, art or method[.]"

The present case is analogous to *Schein* where the USPTO and the Federal Circuit have de facto rewritten Title 35 U.S.C. §101 into an unrecognizable form by insisting a claim must represent "transformation," which this court expressly rejected as a requirement to patentability in *Bilski*.

The USPTO and the Federal Circuit have also de facto rewritten §101 into an unrecognizable form by insisting a claim must represent some form of

"invention," which this Court stated was meaningless as far back as the late nineteenth century (*McClain v. Ortmayer*, 141 U.S. 419 (1891)), and more recently rejected the term as requirement to patentability in *Deere*.

The two most significant changes of the 1952 Patent Act were: (1) to codify the holding of *Hotchkiss v. Greenwood*, 11 How. 250 (1850), so as to define patentability (not "invention") in terms of nonobviousness under 35 U.S.C. §103; and (2) to replace the word "act" under then 35 U.S.C. §31 (Pet.App 62a) with "process" under §101 while defining the word "process" in §100.

The recent *Schein* holding stated it is not within the courts' powers to *de facto* rewrite a single word of the statutory patent laws, or to replace congressional intent with biases the courts feel better suited to patent law. Thus, *it is not within the Constitutional powers of the courts to place a single additional burden on patentability that Congress did not sanction in its statutes*.

While courts may interpret particular words in view of congressional intent, the Supreme Court repeatedly declared that "[u]nless otherwise defined, 'words will be interpreted as taking their ordinary, contemporary, common meaning.'" *Bilski* 603. "Our task… is a narrow one of determining what Congress meant by the words it used in the statute; once that is done, our powers are exhausted." *Diamond v. Chakrabarty* 318.

B. The Standard of "Transformation" Is Offensive to the Statutory Standard Created by Congress

Noticeably missing from §101 is the word "transformation" as a precondition to "obtain a patent therefor." Also noticeably missing from the USPTO's and Federal Circuit's laments about Petitioner's claims is any discussion as to what standard of "transformation" is sufficient for patent-eligibility.

What is a sufficient "transformation?"

As with "invention," there is no standard of "transformation."

While there may be no "transformation" in the present claims that satisfies the USPTO's sensibilities, without doubt the claimed formulations qualify as a "composition of matter" under §101. The claims recite a man-made mixture of chemical entities from different sources in a defined proportion, and thus clearly fall within the ordinary, contemporary and common meaning of a "composition of matter" under §101.

This finding does not depend on the casing feature but is inherent and sufficiently defined by the mixture of substances from different sources alone.

Further, the "casing" limitation also falls within the definition of a "manufacture" according to the ordinary, contemporary and common meaning of "manufacture" as in §101.

Still further, the claims represent an important new and useful discovery in nutrition, and the Federal Circuit has de facto removed the word "discovers" from §101.

The Federal Circuit's treatment of §101 is a rewrite as follows:

> "Whoever invents ~~or discovers~~ any new and useful ~~process~~ transformation, machine, ~~manufacture, or composition of matter,~~ or any new and useful improvement thereof, may obtain a patent therefor."

This re-write of §101 is an instance of extraordinary usurpation of judicial powers from interpreting statutes to completely redrafting them. It is most disturbing that the USPTO and Federal Circuit unlawfully abrogated the "discovery," "process," "composition of matter," and "manufacture" language actually found in 35 U.S.C. §101 from numerous claims at issue in favor of vague concepts that this Court expressly rejected in *Deere* and *Bilski* decisions.

C. The Legislature Set the Statutory Requirements of the APA Based on Separation of Powers

The Supreme Court's decision in *Dickenson v. Zurko*, stressed "the importance of not simply rubber-stamping agency fact-finding." *Id* 162. "The APA requires meaningful review[.]" *Id.*

The Federal Circuit is compelled by Title 5 U.S.C. §706 to hold unlawful and set aside any action, finding, and conclusion by the UPSTO that is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." However, rubber-stamping USPTO the Federal Circuit refused to abide by the express statutory text of §101, which Congress passed, and the President signed in its

present form both in 1952 and 2011. Thus, the USPTO and Federal Circuit have engrafted conditions contrary to statute and this Court's precedent.

This is judicial usurpation of power and an abuse of discretion by both the USPTO and the Federal Circuit. Accordingly, mandamus is warranted to remind them that they are required to abide by Title 35 U.S.C. §101 and Title 5 U.S.C. §706.

Petitioner has every right to expect the USPTO and Federal Circuit to follow statute and established case law. It is a basic principle of fairness and due process that the government must follow the government's own rules.

III. USPTO's and Federal Circuit's Patent Eligibility Analysis Under §101 is Not Based on Preemption But On Faux Product-by-Process Construction

There is a distinct difference in patent eligibility analyses under §101 that is often not understood.

The first type of analysis is whether something is patent-eligible under §101 by virtue of the definitions recited in §100. An example of such an analysis is found in *In re Nuijten,* 500 F.3d 1346 (Fed. Cir. 2007) (holding that an electromagnetic carrier *per se* is not a process, machine, manufacture or composition of matter as recited in §101 and defined by § 100(b)). *In re Nuijten* reflects an example of man-made invention that, as a categorical rule (not categorical exception), falls outside §101.

The second type of analysis addressed in *Alice Corp. v. CLS Bank*, 134 S. Ct. 2347 (2014), is a determination of whether a claim on the whole constitutes an *exception* to §101 by preempting a law of nature, a natural phenomenon, or an "abstract idea." Present claims pass *Alice'* first step/test of patent-eligibility being drawn to "composition of matter" and "process", the question of "additional elements" and "transformation" in Alice's second step/test does not arise. *Alice* 2355.

The present case is not based on *exception*, but upon the notion that under product-by-process construction, the present claims do not constitute a "process" under §101 because there is no "transformation" or "invention" embedded within the claims. (Pet.App 13a, 27a-32a).

IV. The Petitioner's Alleged "Product-by-Process Claims Constitute a Process under §101

"[a]t least one casing [comprising] an intermixture of lipids from different sources" is a required feature of claims at issue. Such a "casing" with the appropriate "intermixture" does not occur in nature, and there is no assertion to the contrary by USPTO or the Federal Circuit.

Furthermore, "dosage" refers to "determination of amount to be administrated"[10], which is also a process under § 100(b).

Without question some man-made process is required to produce the formulation of present claims.

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[10] Fed.Cir.App. Appx6413, Appx7858

The 1952 Patent Act replaced the word "act" under then 35 U.S.C. §31 with "process" under §101 while defining the word "process" in §100. Also, "[u]nless otherwise defined, 'words will be interpreted as taking their ordinary, contemporary, common meaning.'" *Bilski* 603.

Bilski decision also recognized there is no known meaning "of the definitional terms 'process, art or method' that would require these terms to be tied to a machine or to transform an article." *Id.*

Black's Law Dictionary (6th Ed.1990) at p.1205 defines "process" to mean: (1) an "art or method by which any particular result is produced;" (2) a "means or method employed to produce a certain result or effect;" and (3) "a definite combination of new or old elements, ingredients, operations, ways, or means to produce a new, improved or old result[.]"

Clearly, "a definite combination of new or old elements, ingredients, operations, ways, or means to produce a new, improved or old result" describes Petitioner's claims comprising process. A categorical rule differentiating Petitioner's claims from other forms of processes is improper. Such "categorical rule[s] denying patent protection for 'inventions in areas not contemplated by Congress… would frustrate the purposes of the patent law.'" *Bilski* 605 (citing *Chakrabarty*).

Federal Circuit implicitly approved USPTO's product-by-process construction of present claims. Petitioner disagrees with this construction. However, even if the present claims may be construed as a product-by-process, the Federal

Circuit's holding is still erroneous as Petitioner's claims would still include a "process" under §101.

It should not be missed that the term "product-by-process" includes the word "process," and "process" is one of the express categories of patent-eligibility under §101. This is more than a mere game of semantics. One does not derive a new, useful and non-obvious *man-made* "product" without a "process." Of course, the "product" comprising "process" after meeting the §101 thresholds must undergo §102 and §103 tests. Therefore, it is flawless that process steps are patent-eligible under §101.

V. Funk Brothers Holding Relies on the term "Invention," Which the Supreme Court Repeatedly Condemned as Impermissibly Vague and Congress Wrote Out of the Patent Law in 1952.

The opinion below states "The Board held that admixture with other natural products of known composition was *not shown or stated to change the nature of the compositions*, citing *Funk Bros... we agree, that the Applicant has not shown that the claimed mixtures are a 'transformation' of the natural products."* (Pet.App. 11a, 13a).

However, as stated above there is no known meaning "of the definitional terms 'process, art or method' that would require these terms to… transform an article." *Bilski* 603.

The 1952 Patent Act was enacted in response to the Supreme Court's anti-patent sentiment in the early 1900s. This anti-patent sentiment was reported by Karl Lutz (*The New 1952 Patent Statute*,

35:3 Journal of the Patent Office Society, 155, 156-7 (1953)), stating the 1952 Patent Act was enacted to remove "the recent apostasy" of the Supreme Court "from the benevolent policy of the Constitution." Indeed, the "apostasy" pre-1952 was so harsh that Justice Jackson criticized the Supreme Court's "strong passion" for striking patents down "so that the only patent that is valid is one which this Court has not been able to get its hands on." *Jungersen v. Ostby & Barton Co.*, 335 U.S. 560, 572 (1949).

The *Funk Brothers* decision was decided at the height of the pre-1952 "apostasy," and its use of the word "invention" was offensive to Congress, because the term "invention" is meaningless and lacks clarity.

"Invention" lacks so much clarity that Congress and vast numbers of prominent attorneys and legal organizations conspired to rid the country of the word by codifying the 1952 Patent Act. See "*Efforts to Establish a Statutory Standard of Invention: Study of the Subcommittee of Patents, Trademarks, and Copyrights of the Committee on the Judiciary*" United States Senate; Eighty-fifth Congress, First Session Pursuant to Senate Resolution 55, Study No. 7 (published 1958) (hereinafter "the 1958 Study").

Charles Kettering, who headed the National Patent Planning Commission, remarked "[o]ne of the greatest technical weaknesses of the patent system… is the lack of a definitive yardstick as to what is invention" (the 1958 Study, p.2).

The legendary Giles Rich remarked about the difficulty of overcoming the idea of invention concluding "[s]o long as invention is there they can say it isn't good enough to be an invention" (the 1958

Study, p.4). Judge Rich, one of the primary drafters of the 1952 Patent Act, went on to say:

> "The Patent Act of 1952 expresses this [Section 103] prerequisite to patentability without actual reference to "invention" as a legal requirement. Nowhere in the entire act is there any reference to a requirement of "invention" and the drafters did this deliberately in an effort to free the law and lawyers from bondage to that old and meaningless term. The word "invention" is used only to refer to the thing invented. That is why the requirement of "invention" should be referred to, if at all, only with respect to that which is dead." *Id.* 89.

Thus, at the behest of Congress the two primary authors of the 1952 Patent Act, Giles Rich and "Pat" Frederico, replaced "invention" with nonobviousness and, according to Judge Rich, Congress intentionally replaced the phrase "lack of invention" in the law with "nonobvious subject matter." See Rich, Giles, *Laying the ghost of the "Invention" Requirement*, 1:1 APLA Quarterly Journal, pp. 26-45 (1972) (reprinted with permission in *Nonobviousness – The Ultimate condition of Patentability* at p.1:506). Judge Rich expressly stated:

> "The first policy decision underlying Section 103 was to cut loose altogether from the century-old term 'invention." It really was a term impossible to define, so we knew that any effort to define it would come to naught. Moreover, it was felt that so long as the term continued in use, the courts would annex to its

> accretion of past interpretations, a feeling history has shown to be well-founded… So Section 103 speaks of a condition of *patentability* instead of 'invention.'… As compared to finding or not finding 'invention,' Section 103 was a whole new way of thinking and a clear *directive* to the courts to think that way." (emphasis in original) Supra at p.1:508.

Judge Rich's words were echoed in *Graham v. John Deere*, where this Court recognized "[t]he truth is, the word ['invention'] cannot be defined in such manner as to afford any substantial aid in determining whether a particular device involves an exercise of the inventive faculty." *Deere* 11. (Quoting *McClain v. Ortmayer*) "Its use as a label brought about a large variety of opinions as to its meaning both in the Patent Office, in the courts, and at the bar. The *Hotchkiss* formulation, however, lies not in any label[.]" *Id.* 12. "Congress used the phrase 'Conditions for patentability; *non-obvious subject matter*' (italics added), thus focusing upon 'nonobviousness,' rather than 'invention.'" *Id.* 14. "Congress has emphasized 'nonobviousness' as the operative test of the section, rather than the less definite 'invention' language of Hotchkiss[.]" *Id.* **"We believe that strict observance of the requirements laid down here will result in the uniformity which Congress called for in the 1952 Act."** *Id.* 18. (emphasis added).

Thus, this Court cannot now stand by a meaningless standard that originated in 1851, was declared useless by this Court in 1891, rejected by

Congress in 1952, and disavowed by this Court in 1966.

In the last four years the Federal Circuit has *never* reversed a §101 rejection from the USPTO.

Not once!

Under the standard of "invention," the USPTO and Federal Circuit together perfected the apostasy that Justice Jackson criticized nearly seventy years ago in *Jungersen* that the 1952 Patent Act was enacted to cure.

"Invention," being meaningless, has no place in the patent law. It's past time this Court remind the USPTO and the lower courts that they are not entitled to re-write the actual text of Congress' statutory scheme – especially when such redrafting is inconsistent with this court's precedent.

The USPTO's and Federal Circuit's presumptive use of "invention" against Petitioner is a violation of statutory law, legislative intent, and this Court's direction in *Deere* and *Bilski*.

VI. The USPTO's and Federal Circuit's Interpretation of §101 Violates Supreme Court Precedent in Bilski v. Kappos and Graham v. Deere

The Supreme Court's decision in *Bilski v. Kappos* set forth a number of important legal principles that USPTO and the Federal Circuit have ignored for the last eight years. The first principle is the abrogation of the machine-or-transformation test as the appropriate test for patent eligibility under §101. The second principle, related to the first, is this

Court's recognition that there is no definition of "process" that requires a machine or transformation for patent eligibility under §101. Yet this case demonstrates it is the position of the USPTO and the Federal Circuit some "transformation" is necessary for a process under §101.

The USPTO's and Federal Circuit's opinions are based upon the ersatz need for "invention" and "transformation" warranted in *Funk Bros.* (1948).

A writ of mandamus does not require reversal of *Funk Bros.* To the contrary, granting a writ of mandamus merely requires recognition that the 1952 Patent Act substantively changed the standard of patent-eligibility, and that proper claim construction principles discussed in *Bilski* provide clear recognition that the holding of *Funk Brothers* is superseded by statute. There is no issue of *stare decisis* with regard to *Funk Bros*. There is no decision or underlying principle for the Supreme Court to stand by because Congress, using its authority under Article I, Section 8, of the Constitution, changed the standard of patent-eligibility nearly seventy years ago.

In view of the change of statutory law since *Funk Bros.*, the decision below undoubtedly embodies an erroneous categorical rule that treats Petitioner's claims as falling outside the scope of §101 by ignoring the ordinary, contemporary and common meaning of the statutory wording in 35 U.S.C. §100 and §101.

Another reason to reverse the decision below is because the USPTO and Federal Circuit's holdings violate this Court's holding in *Graham v. Deere*,

where the Supreme Court expressly recognized that "invention" has no part in the principles of patent eligibility beyond the test for obviousness under 35 U.S.C. §103.

Stare decisis of *Bilski* and *Deere* requires this Court to grant mandamus.

VII. The Federal Circuit's Inability to Follow Supreme Court Precedent Is Detrimental to Innovation

Decisions like *Funk Brothers* were the impetus of the 1952 Patent Act, which was passed to rid the country of the stifling effects *Funk Brothers* and other such cases had on innovation. By reverting to pre-1952 standards of patent eligibility while ignoring Supreme Court precedent, the Federal Circuit's jurisprudence threatens the stability and reliability of the patent system.

Since *Bilski*, the U.S. patent system has dropped to No. 12 in patent protection and "joins a handful of other countries that are not thought of as being particularly intellectual property friendly."[11] The United States Chamber of Commerce's Global Innovation Policy Center reports the U.S. presently "faces a growing level of uncertainty for innovators, particularly in relation to patent protection."[12] The Federal Circuit now uses the vague idea of "invention" to justify conclusory statements having

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[11] https://www.ipwatchdog.com/2018/02/08/u-s-patent-system-falls-12th-place-chamber-global-ip-index-2018/id=93494/

[12] http://www.theglobalipcenter.com/wp-content/uploads/2018/02/GIPC_IP_Index_2018.pdf at p. 157

no basis in the statutory language of §101. See, e.g., *In re Villena*, Appeal No. 17-2069 (Fed. Cir. 2018).

Innovation is waning, and even the Director of USPTO recognizes the patent system is unstable.[13]

Petitioner asserts these detrimental effects are not caused by the lower courts following Supreme Court precedent, but by the lower courts failing to follow statutory law, standard claim construction practices, and this Court's precedent.

VIII. USPTO's and Federal Circuit's Holding Is Unlawful and Detrimental to Nutrition Science

This case is an analog to *Bilski*. While *Bilski* addressed the patentability of business methods, this case addresses the patentability of nutrition science. However, unlike *Bilski*, directed to an extremely old process, *Bhagat* is directed to a new, specifically-tailored innovation to nutrition pertaining to poorly understood factors, mass confusion, and great potential to enhance public health (Pet.App. 85a-133a).

Innovation should be liberally encouraged in nutrition science as nutrition addresses a wide variety of preventable chronic diseases costing the country hundreds of billions of dollars every year. Accordingly, nutrition science promises potential benefits for individual and public well-being and national economics.

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[13] https://www.law360.com/articles/1032230/uspto-head-calls-for-new-path-to-restore-patent-stability

However, despite the known and unknown benefits of nutrition science, the Federal Circuit takes an unreasonable position that without some nebulous standard of transformation, a new, useful and non-preemptive invention/discovery related to nutrition is not patent-eligible. By insisting on applying the machine-or-transformation test, the Federal Circuit created yet another "categorical rule denying patent protection for 'inventions in areas not contemplated by Congress… "frustrate[ing] the purposes of the patent law.'" *Bilski* 605.

IX. The Application of Lipid Science is Important Humanitarian Issue, and The Bias Against It Is Unconscionable

The invention of extracting food oils for their lipid benefits is approximately 6000 years old. Pet.App. 87a-88a. However, to date random oils are randomly added to foods, there has *never* been any teaching that different batches of same oil (e.g., olive oil) can have significantly different lipid composition or that minor lipid components present in oils can have potent health effects. Oil processing technology for food consumption has "advanced" but delivery of dosages of lipids using different sources for the promotion of health is considered patent ineligible by the USPTO and Federal Circuit.

Extensive evidence has been submitted to USPTO and Federal Circuit that inappropriate intake of amounts/ratios of omega-6 and omega-3 fatty acids cause increased risks of cancer, cardiovascular disease, and inflammatory and autoimmune diseases and that the subject matter is poorly understood. See, e.g., Bhagat and Das, *"Potential role of dietary*

lipids in the prophylaxis of some clinical conditions" Arch Med Sci 2015; 11, 4: 807–818 (Pet.App. 90a-133a). See also, William Harris et al., *Omega-6 Fatty Acids and Risk for Cardiovascular Disease*, 119 Journal of the American Heart Association 902-907 (2009) [14] and Baum et al*., "Fatty acids in cardiovascular health and disease: A comprehensive update"* Journal of Clinical Lipidology (2012) 6, 216–234[15]. Consequently, 117 million Americans live with chronic diseases associated with imbalanced lipid intake, and approximately $3 trillion annually is spent in US on treating those diseases and 1.4 million Americans die of such diseases every year[16], and the confusion and mayhem in the art is still prevalent. [17] The potential public health benefits from this innovation impressively "outweigh the restrictive effect of the limited patent monopoly." *Deere* 11.

This case demonstrates there is an actual bias against healthful inventions and discoveries in nutrition, compared to food product inventions that are notoriously unhealthful.

For example, the patenting of partially hydrogenated oils for human consumption, which started in 1903 [18] is still ongoing. See, e.g., U.S. Patent 9,351,502 ("Oxidized and partially hydrogenated oil or fat" issued May 31, 2016); U.S.

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[14] Fed.Cir.App. Appx205-207
[15] Fed.Cir.App Appx4728-4746
[16] Fed.Cir.App. Appx7692
https://www.cdc.gov/chronicdisease/about/costs/index.htm
[17] Fed.Cir.App. Appx4402-4411
https://en.wikipedia.org/wiki/Omega-6_fatty_acid
[18] https://en.wikipedia.org/wiki/Crisco

Patent Application 2019/0030102 ("Hydrogenation of Cannabis Oil").

The willingness to patent such products is evidence the patent process is friendly to technologies that pose serious harm to human condition. Petitioner has correctly asserted that "structurally altered molecules (e.g. hydrogenated fats) favored by the patent practice have previously caused worldwide diseases for over 100 years." Pet.App. 88a.

The U.S. Food and Drug Administration ("FDA"), though late to the table, agrees. The FDA now requires all food companies to phase out artificial trans fats/hydrogenated oils.[19] The most damning statement made by the FDA is these substances "are not 'generally recognized as safe' (GRAS) for use in food."[20]

Yet despite the horrendous condemnation that trans fats/partially hydrogenated oils are not "generally recognized as safe," there was and is no apparent resistance by the USPTO or the courts to patenting them.

But the government resists advancements in the art of nutrition with the potential of an enormous net benefit to society. "During the nine [now ten] years [the present] patent application has been pending, 13.6 [now 15] million Americans have died of associated chronic diseases." Pet.App. 89a.

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[19] https://www.fda.gov/Food/IngredientsPackagingLabeling/FoodAdditivesIngredients/ucm449162.htm

[20] Supra

Denying patent protection on such significant advances, which will not take place without patent protection, goes against everything the patent system is supposed to promote. Denying patent protection also is facially unconscionable given there is no reason under any section of the Title 35 to deny protection to at least claims 102, 107 and 119, and the express language of §101 clearly indicates that Petitioner's technology is within the bounds of patent-eligible subject matter.

Petitioner's peer-reviewed published research (Pet.App. 90a-133a) demonstrates delivery of properly administered lipids within prescribed ratios/dosages have beneficial effects.

Even if the claimed solutions are not a panacea, they offer an inexpensive humanitarian solution to harrowing public health issues and national health care burden. It is the purpose of the patent system to promote the useful arts in a way that encourages accumulation of discoveries and social betterment.

Accordingly, this Court should grant mandamus, which not only will force the USPTO and Federal Circuit to comply with statutory law but will have the additional benefit of promoting humanitarian benefit.

X. Review Is a Simple Question of Law Requiring Minimal Judicial Resources

Within minutes of review with minimal judicial resources this Court can ascertain:

a) §101 rejection of *all 55 claims* is *indisputably* improper at least because by

USPTO's own admittance the claims comprise process steps;

b) §102 rejection of Claim 82 (and dependent claims) over olives is *indisputably* improper at least because olives are *not* an "intermixture of lipids from different sources:"
c) §102 rejection of Claim 91 (and dependent claims) over walnuts is *indisputably* improper at least because walnuts are *not* an "intermixture of lipids from different sources;" and
d) §102 rejection of Claim 65 and dependent claims over mark is *indisputably* improper at least because Mark does *not* function as "casing comprises an intermixture of lipids from different sources."

Further, mandamus must be granted at least on the basis of Claims 102, 107, and 119, which are solely rejected under §101. It is evident from the plain words of the claims that they constitute a "composition of matter," a "process," and a non-natural "manufacture" within the ordinary, contemporary and common meaning of §101.

Beyond these simple realizations that take minutes to confirm, no more is required for this Court than to apply its own precedent set forth in *Schein v. Archer and White*, *Graham v. Deere*, and *Bilski v. Kappos*.

XI. Granting Mandamus Is Appropriate According to Supreme Court Precedent

There is judicial precedent and statutory support compelling this Court to grant mandamus. The case meets all the requirements for mandamus set out in *Cheney* and encompasses *both* "judicial usurpation of power" and "clear abuse of discretion."

The USPTO's position amounts to an astounding denial that §101 no longer recites that "compositions of matter" and/or a "manufacture" are patent-eligible categories under §101, and that faux standards of patent-eligibility (specifically "invention" and "transformation") rejected by Congress in the Patent Act of 1952 supersede the clear statutory language Congress adopted and this Court expressly recognized in *Deere* and *Bilski*.

The factors for mandamus are readily satisfied. Given there are no rejections of dependent claims 102, 107 and 119 other than under §101, and the subject matter of Petitioner's claims clearly falls under §101, Petitioner has established a "clear and indisputable" right to relief. *Cheney* 381.

Further, given the USPTO's monopoly on granting patents, Petitioner has "no other adequate means" to "attain the relief" Petitioner seeks given USPTO and the Federal Circuit refuse to abide by statutory language that has been law for nearly seven decades.

Finally, the statutory framework of the APA makes clear that "the writ is appropriate under the circumstances." Specifically, §702 of the APA provides that "[a] person suffering legal wrong

because of agency action, or adversely affected or aggrieved by agency action within the meaning of a relevant statute, is entitled to judicial review thereof." Further, §706 of the APA mandates that "[t]he reviewing court shall – (1) compel agency action unlawfully withheld or unreasonably delayed."

Thus, the statutory framework established by Congress demonstrates mandamus is appropriate under the circumstances.

Accordingly, all factors outlined in *Cheney* are satisfied.

XII. Granting Mandamus Will Have a Positive Effect on the Courts and USPTO

Granting mandamus on the very clear and simple issue before this Court will provide an indispensable, reminder to lower courts and USPTO that Congress is solely authorized to determine the categories of patent eligibility. Presently, the USPTO and the Federal Circuit are in complete disarray with respect to patent eligibility under §101 because of the word "invention" and because the USPTO and Federal Circuit refuse to abide by *Bilski*'s declaration that no acceptable definition of "process" requires "transformation." The cure to this chaos is granting mandamus, which will provide a simple reminder that the courts and USPTO are limited to interpreting the plain language of §101, rather than fabricating nonsensical categorical exceptions to patent eligibility that contradict the express language of §101.

CONCLUSION

Both "transformation" and "invention" are *ultra vires* creations having no basis in the statutory framework Congress created. This amounts to USPTO and Federal Circuit *de facto* re-writing the Patent Law. These unlawful acts cannot be reconciled with the *Schein* decision.

Under every conceivable analysis, the claims at issue fall within the statutory framework of §101, and a decision to the contrary not only usurps the Legislature's sole power to determine patent-eligibility but sets precedent dangerous to the stability and reliability of the patent system.

Accordingly, Petitioner respectfully requests this Court issue a writ of mandamus to compel the Federal Circuit to set aside the opinion below and reverse USPTO's arbitrary and capricious decision per statutory standard and this Court's precedent.

At a minimum, this Court should hold this petition pending until resolution of HP Inc. v. Berkheimer, No. 18-415, and Kamran Asghari-Kamrani v. United Services Automobile Association, No. 18-1088, or make it a companion case.

March 22, 2019

Respectfully submitted,

/s/ Urvashi Bhagat
Urvashi Bhagat
Pro Se Petitioner

ANNEX O:

Amicus Brief in Support of Writ of Mandamus (case no. 18-1274),
May 3, 2019

No. 18-1274

In the
Supreme Court of the United States

IN RE URVASHI BHAGAT
Petitioner,

On Petition for a Writ of Mandamus to the United States Court of Appeals for the Federal Circuit

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Amicus Brief of Mr. Marcos Gonzalez in Support of Petitioner Urvashi Bhagat

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Questions before This Court

This case raises fundamental issues concerning patent eligibility under 35 U.S.C. § 101, including:

Is the Federal Circuit entitled to de facto re-write of the statutory text of 35 U.S.C. § 101?

Is Federal Circuit entitled to ignore this Court's holdings of *Diamond v. Diehr,* 450 U.S. 175 (1981) and *Bilski v. Kappos*, 561 U.S. 593 (2010)?

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I. Identity and Interests of Amici Curiae, and Motion for Leave to File

The Amicus Curiae is an independent inventor who specializes in algae-based technologies. Amicus Curiae has a particularly strong interest in the development of appropriate standards for evaluating patent-eligibility under 35 U.S.C. § 101 where naturally-occurring materials are used. Amicus Curiae respectfully urges the Court to grant Urvashi Bhagat's Petition and to reverse the Decision below. Amici Curiae has no stake in the parties or in the outcome of the case beyond the deleterious effects of the instant Decision.[1]

Pursuant to Rule 37.2(b), Amicus respectfully requests leave to submit this amicus brief given the Respondent has not replied to Amicus' timely request or subsequent reminder.

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[1] No party's counsel authored this brief in whole or part; no party or party's counsel contributed money intended to fund preparing or submitting the brief. No person other than the *Amici Curiae* or its counsel made a monetary contribution to its preparation or submission.

Amicus Curiae provided notice to both parties of intent to file an amicus brief on April 24, 2019, on behalf of Petitioner Bhagat, which is at least 10 days prior to the May 4, 2019, filing deadline as required under rule 37(2)(a). Petitioner provided her consent, but Respondent failed to respond.

II. Reasons to Grant Mandamus

The reason to grant mandamus is simple: the Federal Circuit's holding violates the statutory language of § 101, and the Supreme Court's holdings in *Bilski v. Kappo*s and *Diamond v. Diehr*. What was done to Petitioner was an inexcusable, lawless, and immoral violation of law. The decision below does flagrant violence to the law of patent eligibility and to the reputation of the courts.

III. Argument

A. Applicable Statutory Patent Law

Article I, Section 8, of the United States Constitution states "***Congress*** shall have power . . . to promote the progress of science and useful arts" (emphasis added). To this end, ***Congress*** enacted several different acts over time including the 1952 Patent Act and the America Invents Act (AIA).

Section 101 of both Acts states: "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor . . . ."

While it is fully within the courts' powers to identify exceptions under § 101, it is not within the courts' powers to *de facto* rewrite a single word of the statutory patent laws, or to replace congressional intent with biases that the courts feel better suited to patent law. That is, *it is not within the constitutional powers of the courts to place a single*

additional burden on patentability that Congress did not sanction in its statutes.

While courts may interpret particular words in view of congressional intent, the Supreme Court repeatedly declared that "[u]nless otherwise defined, 'words will be interpreted as taking their ordinary, contemporary, common meaning.'" *Bilski v. Kappos,* 561 U.S. at 603. "Our task . . . is the narrow one of determining what Congress meant by the words it used in the statute; once that is done, our powers are exhausted." *Diamond v. Chakrabaty*, 447 U. S. 303, 318 (1980).

B. Applicable Statutory Administrative Law

Proceedings of the Board are governed by the APA, Title 5, §§ 551 et seq. *Allentown Mack Sales & Serv., Inc. v. NLRB*, 522 U.S. 359, 374 (1998). Section 706 of the APA recites:

> "To the extent necessary to decision and when presented, the reviewing court shall decide all relevant questions of law, *interpret constitutional and statutory provisions*, and determine the meaning or applicability of the terms of an agency action. The reviewing court shall—
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> (2) hold unlawful and set aside agency action, findings, and conclusions found to be—
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> > (A) *arbitrary, capricious*, an abuse of discretion, or *otherwise not in accordance with law*" (emphasis added).

The Supreme Court's decision in *Dickenson v. Zurko*, 527 U. S. 150 (1999) stressed "the importance of not simply rubber-stamping agency fact-finding." *Id* at 162. "The APA requires meaningful review[.]" *Id.*

C. The Petitioner's Claims Are Patent Eligible under the Express Statutory Language Congress Set Forth in § 101.

As is stated by the Federal Circuit (Appx 12a, 14a):

> "The Board held that admixture with other natural products of known composition was *not shown or stated to change the nature of the compositions*, citing *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 131 (1948).
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> The Board found, and we agree, that the Applicant has not shown that the claimed mixtures are a '***transformation***' of the natural products, or that the claimed mixtures have properties not possessed by these products in nature" (emphasis added).

The Federal Circuit's holding in the present case is not based on the statutory language of § 101 but instead is based upon the idea that Petitioner's claims do not include an adequate "transformation."

As stated above, 35 U.S.C. § 101 recites: "Whoever invents or discovers any new and useful

process, machine, ***manufacture***, or ***composition of matter***, or any new and useful improvement thereof, may obtain a patent therefor . . .” (emphasis added).

No one disputes that Urvashi Bhagat’s claims satisfy the “manufacture” or “composition of matter” categories expressly embedded in the statutory text of § 101.

Absolutely no one.

The USPTO and Federal Circuit, however, chose to ignore, without so much as an excuse or acknowledgment, that statutory language which undeniably grants Petitioner’s claims patent eligibility.

The question thus arises: How can a total of almost twenty government lawyers between the USPTO and the Federal Circuit (which includes the judges’ clerks) be so ignorant of the text of § 101 that they all just missed the fact that there are four separate categories of patent-eligible subject matter mentioned in § 101 and none of them are “transformation?”

Petitioner Bhagat has every right to expect the USPTO and Federal Circuit to follow the requisite statutory language and not de facto rewrite whatever they choose.

Every person before the courts has that same right, yet in the present circumstances the Federal Circuit denied Urvashi Bhagat the requisite care and consideration.

The Federal Circuit’s § 101 jurisprudence is in dangerous disarray. Indeed this Court could strain all its considerable resources and never find a single

law review or industry article complimenting the Federal Circuit's § 101 jurisprudence.

According to the Federal Circuit, a result of a process must "have properties not possessed by these products in nature." Yet if this is the standard very little is patent-eligible. Gold exists in nature, yet a new and useful process that flattens gold into a thin foil cannot be patent-eligible because the flattened gold has no new properties not found in nature. Similarly, a new and useful method for converting electrical energy from one voltage to another voltage is not patent-eligible because the properties of electrical energy are not changed.

"Transformation" is not a standard for patent-eligibility, and the essential meaningless of the term is one reason "tramsformation" is not included in § 101.

"Transformation" is the Federal Circuit's defiance of this Court's holding in *Bilski v. Kappos* where this Court stated that there is no known meaning "of the definitional terms 'process, art or method' that would require these terms to . . . transform an article." *Bilski*, 561 U.S. at. 603.

Forgetting for a moment that "transformation" is not a standard of patent eligibility under § 101, how can nearly twenty government lawyers just happen to miss that § 101 may be satisfied by the "manufacture" and "composition of matter" categories expressly contemplated and mentioned by Congress many decades ago?

The rejection of Urvashi Bhagat's claims under § 101 is not only a shamefully poor revision of statutory texts, it is immoral. Either every single

official involved in this case did not read § 101 when rejecting Bhagat's claims or every single official did not care what § 101 says.

Urvashi Bhagat deserves better than unabashed carelessness and apathy from the USPTO and the Federal Circuit.

A correct holding reversing the decision below does not require a reversal of *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948). *Funk Brothers* was overruled by 1952 Patent Act.

In view of the change of statutory law since *Funk Brothers* was decided, it is the Amicus' position that the Decision below embodies an unlawful categorical rule that treats Petitioner's claims as falling outside the scope of § 101 by ignoring the ordinary, contemporary and common meaning of the statutory wording in 35 U.S.C. § 101.

D. The Federal Circuit's Decision Must Be Set Aside as the Federal Circuit Did Not Consider the Claims as a Whole

Another reason to reverse the decision below is because it violates a rule that this Courts set forth in *Diamond v. Diehr*, *Mayo v. Prometheus*,[2] and *Alice Corp. v. CLS Bank*[3] Specifically, the *Diamond v. Diehr* decision held that, in determining patent eligibility, "claims must be considered as a whole . . .

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[2] *Mayo Collaborative Services v. Prometheus Laboratories*, 566 U.S. 66 (2012)

[3] *Alice Corp. PTY, Ltd v. CLS Bank Int'l*, 134 S.Ct. 2347 (2014)

." *Diehr*, 450 U.S. at 188. *Mayo* v. *Prometheus* later clarified that, not only must claims be considered as a whole, but that all claim limitations must be considered individually and "as an ordered combination." *Mayo*, 132 S. Ct. at 1298. *Alice Corp.* repeated this rule. *Alice*, 134 S. Ct. at 2350, 2351, 2355 and 2359.

When addressing claims as a whole, words cannot be simply written out of a claim. "[T]he words of a claim are generally given their ordinary and customary meaning . . . . [which is] the meaning that the term would have to a person of ordinary skill in the art[.]" *Phillips v. AHW,* 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (citations and internal quotation marks omitted). "[T]he ordinary meaning of a claim term is its meaning to [an] ordinary artisan after reading the entire patent." *Id.* at 1321. (internal quotation marks omitted).

Turning to the instant decision, the PTAB and Federal Circuit both failed to address all claims limitations individually and as a whole, ordered combination. Notably missing from the Federal Circuit decision is any indication that the Federal Circuit considered a single claim as a whole given the lack of any discussion of the hotly-contested "casing" limitation of the independent claims. Indeed, the Federal Circuit refused the slightest comment on the subject.

That is an entirety of a federal administrative agency and the Federal Circuit refusing to follow this Court's clear precedent. This is inexcusable and does violence to years of research by Petitioner as well as the reputation of the USPTO and the judiciary.

IV. The Supreme Court Should Hold Any Decision against Petitioner in Abeyance

The Federal Circuit's Decision is a clear violation of the APA and should be set aside under mandamus. While Amicus understands that this Court's time is beyond valuable, Amicus also observes that there is a wealth of § 101 cases presently before the Supreme Court that share many common issues. Accordingly, should this Court lean to dismissing this Petition, Amicus strongly suggests that this case should be taken into consideration as a companion case as a matter of simple justice given that the additional time necessary to address the wrongs to Petitioner Bhagat would be minimal.

V. Conclusion

The Federal Circuit's Decision is a clear violation of the APA and should be set aside.

Respectfully submitted,

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ANNEX P:

Petition for Rehearing for Writ of Mandamus (case no. 18-1274),
June 7, 2019

No. 18-1274

In the

Supreme Court of the United States

IN RE URVASHI BHAGAT

Petitioner

On Extraordinary Writ of Mandamus to the United States Court of Appeals for the Federal Circuit and the United States Patent and Trademark Office

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PETITION FOR REHEARING

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PETITION FOR REHEARING
&
MOTION FOR LEAVE TO HAVE THE PETITION TREATED AS PETITION FOR REHEARING FILED OUT OF TIME OF THE PREVIOUS PETITION FOR CERTORARI

Pursuant to Rule 44.2 Petitioner requests this Court for rehearing of its petition for mandamus. Though mandamus grants and rehearing grants are sparingly exercised but the conditions are not insuperable. *Cheney v. U.S. District Court*, 542 U.S. 367, 380-81 (2004); *Melson v. Allen,* 130 S. Ct. 3491 (2010); *Gondeck v. Pan Am World Airways*, 382 U.S. 98 (1957); and *United States v. Ohio Power Co.*, 353 U.S. 98 (1957).

Alternately, the Court should treat this petition as petition for rehearing filed out of time of the previous petition for certiorari denied on October 29, 2018[1]. In such circumstances, the Court has accepted untimely petitions for rehearing. *Foster v. Texas* No. 131 S. Ct. 1848 (2011); *Gondeck v. Pan Am World Airways*, 382 U.S. 98 (1957). The Court has also treated mandamus petitions as certiorari when warranted. *In Re United States*, 583 U.S. ___ (2017).

"The interest in finality of litigation must yield when the interests of justice would make unfair the strict application of the Rules of this Court." *Ohio Power Co.* 99.

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[1] No.18-277.

CONSTITUTIONAL PROVISIONS INVOLVED

Amendment VIII:

> "Excessive bail shall not be required, nor excessive fines imposed, nor cruel and unusual punishments inflicted."

Amendment XIV:

> "Section 1:
> All persons born or naturalized in the United States, and subject to the jurisdiction thereof, are citizens of the United States and of the State wherein they reside. No State shall make or enforce any law which shall abridge the privileges or immunities of citizens of the United States; nor shall any State deprive any person of life, liberty, or property, without due process of law; nor deny to any person within its jurisdiction the equal protection of the laws."

FACTUAL & PROCEDURAL BACKGROUND

A. Proceedings Below

Petitioner filed the US Patent Application no. 12/426,034 on April 17, 2009, motivated by the suffering and premature death of her own mother, and the finding that millions of people around the world are similarly suffering due to overwhelming erroneous teachings around lipid intake (associated with all chronic diseases) coming from a large body of international scientists including the National

Institutes of Health at the United States Department of Health and Human Services[2] and the popular media[3] and that similarly misdirected lipid teachings have harmed public health for 100s of years and continue to do so. Mand.Pet.35-37[4]. Particularly, the Petitioner found the teachings of low-fat, low omega-6, high omega-3, and high omega-9 (monounsaturated) fatty acids all to be incorrect. Contrary to such teachings, Petitioner found omega-6 to omega-3 ratio greater than 4:1, omega-6 greater than 20% by weight of total lipids, omega-6 at least 11g/day for adults, and omega-9 to omega-6 ratio less than 5:1 to be beneficial for health, wherein dosage of omega-6 fatty acids and presence or absence antioxidants and phytochemicals is material[5]. Realizing the extreme variability and unpredictability of lipids in natural sources (even within the same species, e.g. 9-85% and 4-21% variation in omega-6 content in safflower and olive oils[6]) and less than 1% public understands lipids[7], the Petitioner devised the innovative solution to preformulate lipid dosages from different sources for

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[2] *Simopoulos et al., "Essentiality of and Recommended Dietary Intakes for Omega-6 and Omega-3 Fatty Acids" Ann Nutr Metab 1999;43:127–130*; Fed.Cir.App.4446-4449 (teaching upper limit of omega-6:omega-3 ratio of 2.32:1 and maximum omega-6 intake of 6.67 grams/day for a 2000 kcal diet, ratified by thirty scientists).

[3] WHFoods.com *"A New Way of Looking at Fats"* Jan 2007; Fed.Cir.App.6140-6142 (teaching omega-6 to omega-3 ratio of 2:1)

[4] Petition for Mandamus.

[5] Fed.Cir.App.56-114.

[6] Fed.Cir.App.5472-5474; Fed.Cir.App.5479-5482.

[7] International Food Information Council Foundation, 2011 Food & Health Survey.

tailored delivery to subjects within the preferred dosages and concentrations recited above.

However, in an extreme case of abuse of discretion USPTO rejected *55 claims* (Pet.App.63a-84a) under 35 USC §101 and *52 claims* under §102 of the subject application by excising *many* limitations from *many* claims, because otherwise no rejections could be maintained. From the independent claims 65, 91, 129, and 130, USPTO excised the limitations "dosage" and "casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids [or fatty acids in claims 129 and 130] from different sources", and **despite admitting that the claims comprise process steps, USPTO alleged the claims are by process drawn to products occurring in nature, holding composites of lipids patent-ineligible, and opposite teaching, not well-understood, non-conventional features to be irrelevant**[8]**, contrary to** *Mayo Collaborative Servs. v. Prometheus Labs, Inc.,* 566 U.S. 66 (2012) and *Alice Corp. v. CLS Bank,* 134 S. Ct. 2347 (2014). **Claims 102, 107, and 119 were solely rejected under 35 USC §101, despite admitting the combination of elements recited in the claims does not occur in nature**[9]**.**

The United States Court of Appeals for the Federal Circuit **rubber-stamped USPTO, failing to answer almost entirety of Petitioner's arguments and evidence submitted, and failing to even review**

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[8] Fed.Cir.App.11-16.
[9] Fed.Cir.App.7436¶2.

independent claims 91, 129, and 130 and several dependent claims.

B. Proceedings Before This Court

Petition for Certiorari was filed before this Court asserting the Federal Circuit erred in finding Petitioner's claims unpatentable under §101 because the court failed to apply the patent-eligibility standard under this Court's contemporary holding in *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576 (2013). The Petitioner also asserted the Federal Circuit's affirmation of USPTO was erroneous because it failed to apply "meaningful review" required by the Administrative Procedure Act. Yet this Court denied the Petition on October 29, 2018.

On March 30, 2019, the Petitioner filed a Petition for Writ of Mandamus citing **astounding breadth** of abuse of discretion by the Federal Circuit **on every count**:

- failed to review claim construction,
- de facto rewrote §101 to strike, "composition of matter", "manufacture", and "process" from the statute,
- required "transformation" from process steps under §101 contrary to this Court precedent in *Bilski*,
- failed to cite eligibility and anticipation law based upon which the case is decided,
- failed to meaningfully review §102 rejections,
- acknowledged prosecution disclaimer of single source like olives/walnuts, then disregarded it

and affirmed §102 rejection over olives/walnuts anyway,
- failed to review many claims including independent claims, and
- failed to consider eleven expert testimonies[10] cited in petitioner's briefs.

Additionally, Petitioner emphasized Claims 102, 107, and 119 were solely rejected under §101, and USPTO admitted such compositions do not occur in nature. Mand.Pet.7-8, 10, 13.

Thus, Petitioner provided this Court strong reasons and quick review process for mandamus grant, easily exercised under this Court's GVR (grant, vacate, remand) practice.

Yet, this Court denied the Petition for Mandamus on May 13, 2019.

GROUNDS FOR REHEARING

I. THE OPINION BELOW VIOLATES THE PETITIONER'S CONSTITUTIONAL RIGHTS TO EQUAL PROTECTION OF THE LAWS UNDER THE 14th AMENDMENT

A. The Petitioner has a constitutional right to equal protection of laws as this Court provided in *Myriad*

[10] "Testimonies" throughout this petition refers to the eleven testimonies on record listed in the Table of Authorities in this petition.

This Court ruled in *Myriad* that cDNA is patent eligible in spite of arguments that the nucleotide sequence "is dictated by nature, not the lab technician." *Myriad* 595. Stating it is not enough for finding of patent ineligibility to find some of the claim elements in naturally occurring things, and "dictated by nature" is not the test, this Court made clear that not all claims containing "naturally occurring things" are ineligible. *Id.* 589.

Petitioner's claims are farther apart from a product of nature than cDNA because they include features like, "formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4: 1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids from different sources…"

Therefore, as in *Myriad* the fact that some of the claim elements may be found in naturally occurring things is irrelevant and "dictated by nature" is not the test, accordingly instant claims are patent-eligible.

B. The Petitioner has a constitutional right to equal protection of laws as this Court provided in *Bilski*

This Court held in *Bilski v. Kappos,* 561 U.S. 593 (2010) there is no known meaning "of the definitional terms 'process, art or method' that would require

these terms to . . . transform an article." *Bilski* 603. Likewise, there is no requirement in the law that the Petitioner's claimed formulations "comprising a dosage of omega-6 and omega-3…contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids from different sources…" demonstrate anymore "transformation" than is explicitly and implicitly present in the claimed formulations.

The opinion below improperly requires "transformation" from claims comprising "composition of matter", "manufacture", and "process", each independently patent-eligible under §101, accordingly instant claims are patent-eligible.

C. The Petitioner has a constitutional right to equal protection of laws as this Court provided in *Diehr, Mayo,* and *Alice*

In *Diehr* this Court held that, in determining patent-eligibility, "claims must be considered as a whole…" *Diehr* 188. *Mayo* later clarified not only must claims be considered as a whole, but all claim limitations must be considered individually and "as an ordered combination." *Mayo* 79. *Alice* repeated this rule. *Alice* 2355, 2359.

When addressing claims as a whole, words cannot be simply written out of a claim. "[T]he words of a claim are generally given their ordinary and customary meaning… [which is] the meaning that the term would have to a person of ordinary skill in

the art[.]" *Phillips v. AHW*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (citations and internal quotation marks omitted).

In the current case, the PTAB started and Federal Circuit condoned, failing to address all claims limitations individually and as a whole, ordered combination. Mand.Pet.12-14.

Further, this Court has held in *Mayo, Myriad*, and *Alice* that ***not well-understood, non-routine, and non-conventional features,*** as in the current claims (see testimonies), weigh towards eligibility, which the opinion below has completely disregarded.

Accordingly, instant claims are patent-eligible.

II. THE OPNION BELOW IS IN VIOLATION OF THE PETITIONER'S CONSTITUIONAL RIGHTS TO DUE PROCESS AND EQUAL PROTECTION OF THE LAWS UNDER 14th AMENDMENT

The required elements of due process are those that "minimize substantively unfair or mistaken deprivations" by enabling persons to contest the basis upon which a state proposes to deprive them of protected interests. *Fuentes v. Shevin*, 407 U.S. 67, 81 (1972).

A. The Federal Circuit failed to cite law based upon which the claims are patent-ineligible and anticipated. Businesses can no longer rely on clear rule of law, defining, "like the metes and

bounds of a deed," the conduct which is required[11].

B. The Federal Circuit failed to even review independent claims 91, 129 and 130.

C. The Federal Circuit failed to base its opinion ***upon record***, as per this Court's precedent in *Goldberg v. Kelly*, 397 U.S. 254, 271 (1970), disregarding arguments to proper claim construction, and *testimonies* of skilled persons as to their interpretation of the claim terms, variability in nature, poorly understood factors, and lack of anticipation due to ambiguity and temporal context.

D. The Federal Circuit disregarded *eleven testimonies* from skilled persons evidencing poorly understood factors in this case, in contrast to its own ruling in *Berkheimer V. HP Inc., 881 F. 3D 1360* (2018) and this Court's ruling in *Microsoft Corp. v. i4i Ltd. P'ship,* 564 U.S. 91, 95 (2011).

> *"The question of whether a claim element or combination of elements is well-understood, routine and conventional to a skilled artisan in the relevant field is a question of fact. Any fact, such as this one, that is pertinent to the invalidity conclusion must be proven by clear and convincing evidence. See Microsoft Corp…" Berkheimer 1368.*

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[11] Petition for Rehearing, *Graver Mfg. Co. v. Linde Co.*, 337 U.S. 910 (1949), 339 U.S. 605 (1956), *reprinted in* Frederick B. Wiener, *Effective Appellate Advocacy* 503-07 (1950).

> *"Whether a particular technology is well-understood, routine, and conventional goes beyond what was simply known in the prior art. The mere fact that something is disclosed in a piece of prior art, for example, does not mean it was well-understood, routine, and conventional…" Id. 1369.*

Yet the Federal Circuit disregarded the *testimonies* and that the cited references whfoods.com and Mark themselves teach the opposite. See *Rustagi, Das, and Rucker* testimony of September 2014 ¶5 ¶10. This evidences Federal Circuit's bias against nutrition and denial of due process and equal justice to *pro se* appellants.

III. THIS COURT'S DENIAL OF THE SUBJECT PETITIONS IS IN VIOLATION OF PETITIONER'S CONSTITUTIONAL RIGHT TO EQUAL PROTECTION OF THE LAWS AS THIS COURT PROVIDED IN DICKENSON

The Supreme Court's decision in *Dickenson v. Zurko*, 527 U. S. 150 (1999) ruled upon "the importance of not simply rubber-stamping agency fact-finding." Id 162. "The APA requires meaningful review[.]" Id. Petitioner has a right to the same.

IV. THERE ARE INTERVENING CIRCUMSTANCES OF A SUBSTANTIAL EFFECT ON THIS CASE AND PREMATURE DENIAL VIOLATES THE PETITIONER'S CONSTITUIONAL RIGHTS TO EQUAL

PROTECTION OF THE LAWS UNDER 14th AMENDMENT

There are three cases currently pending before this Court—Berkheimer (No. 18-415), Vanda Pharmaceuticals (No. 18-817) and InvestPic (No. 18-1199), where the Court is reviewing similar §101 issues.

Though this case should indisputably be remanded, but at the very least this Court should hold this case in abeyance until the above cases are decided.

V. THIS COURT SHOULD PROVIDE CLEAR GUIDANCE TO LOWER COURTS THAT FUNK BROS. IS OBSOLETE

Though it was unclear what law the Federal Circuit applied in deciding eligibility under §101, alluding to *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948) in reference to claim 128 (dependent on unreviewed claim 91).

Funk Bros. is an obsolete law rendered moot by the 1952 Patent Act replacing §31 addressing eligibility and novelty, with §101 addressing eligibility, §102 addressing novelty, and §103 addressing non-obviousness. However, this Court should grant rehearing of the Petition for Writ of Certiorari and address the stark contrast between *Myriad* and *Funk Bros*. because the manner in which *Funk Bros*. is referenced in *Myriad* has obfuscated direction to lower Courts.

In *Myriad* this Court held so long as the cDNA omitted non-coding introns through a routine process, the cDNA was not a natural product. In contrast, in *Funk Bros.* this Court held once the mutually non-inhibitory property of the bacteria were discovered, it would only be a "simple step" to mix them with a known carrier and sell them packaged in combination, and so no inventive act– beyond the discovery of non-inhibition, a natural phenomenon–was involved in the claims.

Funk Bros. with *Myriad* language reads as follows:

> *"But once nature's secret of the non-inhibitive quality of certain strains of the species Rhizobium [or the DNA sequence of an isolated BRCA gene] was discovered, the state of the art made the production of a mixed inoculant [or the production of cDNA] a simple step…All that remains [to support the mixture of strains being a product of invention]…are advantages of the mixture of inoculants [or the cDNA molecules] themselves. They are not enough."*

However, in *Myriad* this Court did not impose any requirement for further inventive act in claims directed to routine production of cDNA from a gene once the gene's sequence was known.

This Court should grant rehearing to the petition for certiorari and simply issue GVR order stating *Funk Bros*. is obsolete.

VI. THE PROCEEDINGS TO DATE VIOLATE THE PETITIONER'S AND PUBLIC'S CONSTITUIONAL RIGHTS UNDER 8th AMENDMENT THAT "CRUEL AND UNUSUAL PUNISHMENTS [SHALL NOT BE] INFLICTED."

This Court refuses to inflict "cruel and unusual punishments" even upon criminals guilty of the most heinous crimes due to the constitutional provision under 8th Amendment. *Kennedy v. Louisiana*, 554 U.S. 407 (2008).

Yet this Court condones "cruel and unusual punishments" inflicted upon millions of innocent civilians every day in form of drugs, devices, and surgeries because the patent system condoned by this Court skews the marketplace in favor of drugs, devices, and procedures.

Almost all chronic diseases are associated with improper intake of lipids as evidenced by 100s of studies conducted in past 100 years (see testimonies). Therefore, when public lipid intake is corrected by delivery of tailored lipid dosages by subject type, the foundation of health is corrected, hormonal balance is corrected, and immunity is strengthened and susceptibility to infections is reduced. Therefore, the subject innovation can substantially reduce the suffering of 117 million

Americans from chronic diseases and of 80% of women from hormonal issues.

Americans are literally put under a knife in cardiovascular surgery, and subjected to drugs and devices in diabetes, because preventative solutions such as tailored lipids are not effectively implemented. For example, why are we throwing medications on people who have mild depression or on young women suffering from premenstrual syndrome, which can be abated with correct lipid delivery? Same with,

- 90 million people suffering from diabetes or pre-diabetes,
- 54 million people with arthritis,
- 26 million people with asthma, and so on...

The Petitioner has also been put through a grueling 10-yearlong prosecution, no less than "cruel and unusual punishment", for attempting to solve a problem, above the personal suffering ordained from prolonged mother's illness due to incorrect teaching on lipids.

THIS COURT SHOULD REFER THIS CASE TO INTERNATIONAL COURT OF JUSTICE (ICJ) FOR FURTHER INQUIRY INTO VIOLATION OF HUMAN RIGHTS DUE TO DYSFUNCTIONAL INTERNATIONAL PATENT SYSTEM

There is a definite bias against nutrition at patent offices worldwide, and when nutritional patents are granted, they are severely restricted

causing more chaos and misinformation. This is how omega-3 got out of hand and hyped out of context.

In order to rise above the noise and make an impact sufficient scope in the patent is necessary, as claimed. The allegation that granting such claims would inhibit research is incorrect. On the contrary, this innovation will spur new downstream research in medicine also that thus far has not received attention because research resources have been usurped in focus on diseases that can be abated by tailored lipids.

Patent offices grant restricted patents because higher number of filings increase revenue. But this keeps public confused and ill, and a system is created that perpetuates confusion. If the patent system inhibits advancement for revenue, then the system is failing.

Prevention reduces healthcare spending and reduction in suffering from diseases increases productivity, per capita income Gross Domestic Product, taxes earned, and benefits nations.

ICJ should investigate violation of human rights from dysfunctional patent system.

CONCLUSION

This Court should grant the petition for rehearing.

June 6, 2019

Respectfully submitted,

/s/ Urvashi Bhagat
Urvashi Bhagat
Pro Se Petitioner

CERTIFICATE OF GOOD FAITH

I hereby certify that this Petition for Rehearing from denial of writ of certiorari and writ of mandamus is presented in good faith and not for delay, and that it is restricted to the grounds specified in Rule 44.2, namely intervening circumstances of substantial or controlling effect and substantial grounds not previously presented.

June 6, 2019

Respectfully submitted,

/s/ Urvashi Bhagat
Urvashi Bhagat
Pro Se Petitioner

ANNEX Q:

Petition for Rehearing for Writ of Certiorari (case no. 18-277), July 11, 2019

No. 18-277

In the
Supreme Court
of the United States

IN RE URVASHI BHAGAT,
Petitioner,

v.

ANDREI IANCU, DIRECTOR, U.S. PATENT AND TRADEMARK OFFICE,
Respondent.

On Petition For a Writ of Certiorari To The United States Court of Appeals for the Federal Circuit

PETITION FOR REHEARING

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Motion for Leave to File Petition for Rehearing Out of Time

In *United States v. Ohio Power Co.*, 353 U.S. 98, 99 (1957) this Court stated "We have consistently ruled that the interest in finality of litigation must yield where the interests of justice would make unfair the strict application of our rules. This policy finds expression in the manner in which we have exercised our power over our own judgments, both in civil and criminal cases."

This is exactly such a case. There is no prejudice or harm caused to the Federal Government in general or specifically to the United States Patent and Trademark Office (USPTO). There are no intervening equities that make the granting of relief inappropriate. There are no circumstances relevant to consideration of the equities of this case that make the granting of relief inappropriate.

In contrast, the USPTO and lower courts have constantly subjected Petitioner Bhagat to ever-shifting standards of law – none of which are consistent with the statutory regime of the Patent Law, this Court's precedent, or Federal Circuit precedent. It is of particular interest that *exactly one day* after the Federal Circuit announced by a near-unanimous *en banc* decision (May 31, 2018) that well-known, routine, and conventional limitations under step two of the *Alice/Mayo* test are to be treated an issue of fact in light of state of the art at the time of the patent under *Berkheimer v. HP, Inc.*, 881 F.3d 1360 (Fed.Cir. 2018), the Federal Circuit refused to hear *Bhagat's* petition on rehearing (Pet.App. 64a-65a) even though it was clear that the Federal Circuit treated Bhagat's claim limitations

beyond the abstract idea as an issue of law and without regard to the state of the art at the time of the patent.

Further, for reasons set forth below, the Supreme Court has for the first time in over five years shown interest in a question that impacts *Bhagat* and that require no additional resources by this Court other than to recognize that resolving *Berkheimer* or *Vanda Pharmaceuticals* resolves *Bhagat*. Still further, as is explained below it has recently come to light that the lower courts are refusing to follow this Court's precedent as an issue of policy in a manner that prejudiced *Bhagat* both in the USPTO and the Federal Circuit.

The equities favor granting this Motion for Leave to File Out of Time.

Revised Question Presented Upon Rehearing

The following is a question that has been inconsistently answered by the lower courts since the two-part eligibility test was first announced in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66, 79 (2012). This question is the central issue pending in *Hewlett Packard, Inc. v. Berkheimer*, Case No. 18-415, and *Hikma Pharmaceuticals v. Vanda Pharmaceuticals.*, Case No. 18-817, and is necessary for this Court to resolve in order to bring consistency to the lower courts.

> Is patent eligibility a question of law based on the scope of the claims or a question of fact based on the state of the art at the time of the patent?

I. Reasons to Grant Certiorari

While the USPTO and Federal Circuit never presented the patent eligibility rejection to Petitioner Urvashi Bhagat formally under the two-part *Alice/Mayo* test (Pet.App. 25a-37a), the patent eligibility question in *Bhagat* is plagued by the same underlying issues as dozens of other *Alice/Mayo* cases previously or presently before this Court. Petitioner Bhagat was just never informed her claims were being evaluated under the *Alice/Mayo* test. Petitioner Bhagat asks what objective standards may patent owners rely upon under step two when confronted by a patent eligibility challenge under the *Alice/Mayo* test assuming that at least one element of a patent claim exceeds a natural phenomenon or other abstract idea. The failures of the Federal Circuit to issue consistent opinions literally one day to the next should not result in a failure by this Court to consistently address the exact same issue presented in *Berkheimer* and *Bhagat*.

This lack of consistency has drawn the attention of the United States Senate. For instance, on June 4, 2019, the (retired) honorable Judge Paul Michel testified before the U.S. Senate Subcommittee on the Judiciary stating:

> "[R]ecent changes to patent case law have produced unending chaos. Uncertainty, unpredictability, inconsistent results and undue and harmful exclusions of new technologies abound. Consequently, patents are considered unreliable by the very people -- business executives and innovation investors like venture capital firms -- who make the

> necessary, but risky, investments. The results point to decreased formation of start-ups, flight of investments to less risky sectors than science and useful arts, migration of innovation investments to foreign jurisdictions with broader eligibility, and many other harms. Together these dynamics threaten our economic growth, productivity increases, job creation, global competitiveness, scientific leadership and even national security.
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> If I, as a judge with 22 years of experience deciding patent cases on the Federal Circuit's bench, cannot predict outcomes based on case law, how can we expect patent examiners, trial judges, inventors and investors to do so?" [1]

Judge Michel's comments are reflected by other distinguished members of the patent community including former Director of the USPTO David Kappos and former Director of the USPTO Todd Dickenson.[2] [3]

Berkheimer and *Bhagat* are an example of (in Judge Michel's words) outcomes to identical issues

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[1] https://www.judiciary.senate.gov/imo/media/doc/Michel%20Testimony.pdf at pp. 3 et seq.

[2] https://www.judiciary.senate.gov/imo/media/doc/Kappos%20Testimony.pdf at p.1.

[3] https://www.judiciary.senate.gov/imo/media/doc/Dickinson%20Testimony.pdf at p. 4.

that are "inconsistent with one another and confusing." Industry needs clarity.

II. It Is the USPTO's Professional Opinion That the Claims at Issue Include Limitations That Are Not Well-Understood, Routine, and Conventional

As an initial issue, it is not contested that the USPTO and the Federal Circuit failed to address all the claim limitations. Indeed, the record clearly shows that they intentionally discounted the "casing" and "dosage" limitations. Pet.App. 5a-6a, 31a.

However, even discounting the casing and dosage limitations, there are three claims (102, 107, and 119) at issue that were rejected under § 101 but not rejected under § 102 or § 103. Pet.App. at 12a. The Petitioner now presents only these three claims for a specific review. Of these three claims, the USPTO argued that there was no appropriate "transformation" (Pet.App. 14a, 36a), which the USPTO considers an issue of law citing *Funk Brothers v. Kalo*, 333 U.S. 127 (1948). Pet.App. 28a-29a.

Thus, it is apparent that if patent eligibility under step two of the *Alice/Mayo* test is an issue of fact based upon a comparison of the prior art (Pet.App. 14a, 36a), claims 102, 107, and 119 are patent eligible.

On the other hand, if step-two of *Alice/Mayo* is resolved as a pure question of law answerable under *Funk Brothers* and *Myriad*, then the USPTO's and Federal Circuit's analysis is still not plausible in light that the 1952 Patent Act overruled *Funk Brothers*. See also *Ass'n for Molecular Pathology v.*

Myriad, 133 S.Ct 2107 (2013) (finding cDNA patent eligible by rejecting a "dictated by nature" test).

However, *Petition declines to argue any legal or factual errors of the Federal Circuit under Rule 10 of the Supreme Court rules*. Petitioner only argues the narrow but highly-contested issue *Bhagat* has in common with both *Berkheimer* and *Vanda Pharmaceuticals*.

III. Unlike *Mayo*, There Is No Admission in the *Bhagat* Specification That the Additional Limitations Are Well-Understood, Routine, and Conventional

The *Mayo* decision makes clear that the Supreme Court had an intrinsic evidentiary basis to determine that various steps beyond the abstract idea lacked an inventive concept. Specifically, the *Mayo* opinion states that the "determining" step – the only step not inherently necessary to practice the abstract idea – was well-understood, routine, and conventional *as is evidenced by the specification*. *Mayo*, 566 U.S. 78-79 ("As the patents state, methods for determining metabolite levels were well known in the art.").

As with contracts and deeds, patents are legal instruments. "A patent is a legal instrument, to be construed, like other legal instruments, according to its tenor." *Markman v. Westview Instruments*, 517 U.S. 370, 388 (1996).

Thus, under the circumstances of *Mayo* this Court addressed step two of the *Alice/Mayo* test using *unrebutted intrinsic evidence*, and the claims were disposed of as an issue of law with all underlying factual issues being satisfied.

Unlike *Mayo*, *Bhagat* makes no such admissions justifying a holding of patent ineligibility. Rather the *Bhagat* specification establishes that the limitations at issue are *not* well-understood, routine, and conventional,[4] which the USPTO disregarded and Federal Circuit left unaddressed (Pet.App. 34a) because they were addressing the Bhagat claims as a pure issue of law.

Thus, as with *Berkheimer* and *Vanda Pharmaceuticals* (which make no admissions justifying a holding of patent ineligibility), the evidentiary burden in all of *Berkheimer*, *Vanda*, and *Bhagat* is not met consistent with Supreme Court precedent.

IV. The *Alice/Mayo* Test Should Be Consistent with the Supreme Court's *Markman v. Westview Instruments* and *Graham v. John Deere* Opinions

Application of Markman and Graham: When addressing patent eligibility it is important that the lower courts treat issues of law and issues of fact in a manner consistent with this Court's teachings outlined in *Markman v. Westview Instruments*. Similarly, *Graham v. John Deere*, 383 U.S. 1 (1966) provides critical and long-uncontested guidance that must be considered.

Turning to the substance of *Markman*, the Supreme Court noted that "the patent itself must be taken as evidence of its meaning; that, like other written instruments, *it must be interpreted as a whole . . .* and the legal deductions drawn therefrom

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[4] See, e.g., Pet.App. 57a-58a, (para [0006]-[0007]).

must be conformable with the scope and purpose of the entire document" (emphasis added). *Markman*, 517 U.S. at 383, n. 8. Thus, it is entirely possible and proper that a judge might take a legal decision based on the intrinsic evidence of a patent specification so long as the legal decision was taken in the context of the patent specification as a whole. *Markman* thus cautions that one sentence out of context does not suffice as an admission.

Further, as Markman shows throughout its text conclusory remarks are not legal conclusions. There is no authority that allows patent examiners and judges to make legal conclusions on what is well-known, routine, and conventional untethered from both evidence and a patent specification as is the current practice of the USPTO and the lower courts when addressing patent eligibility. The Supreme Court has never condoned such conduct.

The *Mayo* decision is a thoughtful example of the above-discussed principles set forth in *Markman*. However, the legal community needs more than example: it needs some express direction of the sort provided in *Markman* and *Graham*.

Turning to issues of fact, it is long settled that patent validity is an issue of law having underlying issues of fact resolved by comparing claims to "the scope and content of the prior art." *Graham*, 383 U.S. at 17. Patent validity is not patent eligibility. However, discerning whether a claimed limitation is well-known, routine, and conventional is unquestionably a comparison of a claim to "the scope and content of the prior art."

Consider *Bilski v. Kappos*, 561 U.S. 593, 611 (2010). The Supreme Court did not merely proclaim the particular business method abstract without evidence. Similarly, the business method of *Alice Corp.* was so ancient it was fully described in a business text from 1896. *Alice Corp. v. CLS Bank*, 134 S.Ct. 2347, 2356 (2014)

Thus, Supreme Court precedent expressly teaches that the *Alice/Mayo* test may be fully reliant on an underlying factual inquiry of the prior art that cannot be satisfied by any reading of a patent specification.

Analysis of *Bhagat* as an Issue of Fact*:* As stated above, discerning whether a claim limitation is well-known, routine, and conventional is unquestionably a comparison of a claim to "the scope and content of the prior art." While this is not to say that an admission in a patent specification cannot be used to satisfy such an inquiry, *Bhagat* offers no such admission. In the present circumstances *Alice/Mayo* becomes a test reliant on a comparison of the claim limitations to the state of the art at the time of a patent.

Analysis as an Issue of Law*:* Addressing the additional claim limitations under step two of the *Alice/Mayo* test as an issue of law, the record shows that the USPTO and the Federal Circuit treated Bhagat's claims under the legal standard of "transformation" and without regard to the scope of the prior art. However, if step two is a pure question of law, Petitioner will not bother this Court with arguments about mere misapplications of law.

V. The USPTO Never Addressed the Claims as a Whole When Addressing the *Alice/Mayo* Test

Supreme Court precedent long holds that, in determining patent eligibility, claims must be considered as a whole, ordered combination. *Diamond v. Diehr,* 450 U.S. 175, 188 (1981); *Mayo*, 566 U.S. at 79; *Alice*, 134 S.Ct. at 2350, 2351, 2355 and 2359.

It is uncontested that the USPTO and the Federal Circuit failed to address the claims as a whole in *Bhagat*. Petitioner asserts that this violation of Supreme Court precedent is not mere error but the rule upon which the USPTO and lower courts operate. This is evidenced by the draft for § 101 reform recently presented by the Senate Subcommittee on the Judiciary, which reads:

> "Section 101:
>
> (a) Whoever invents or discovers any useful process, machine, manufacture, or composition of matter, or any useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.
>
> (b) Eligibility under this section shall be determined only while considering the claimed invention as a whole, without discounting or disregarding any claim limitation." [5]

During the Senate hearings, Scott Partridge, former Chair of the American Bar Association's Section of Intellectual Property Law testified:

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[5] https://www.tillis.senate.gov/services/files/E8ED2188-DC15-4876-8F51-A03CF4A63E26

> "The legislative proposal creates a new subsection (b) under 101 that would stipulate clearly that 'eligibility under this section shall be determined only while considering the claimed invention as a whole, without discounting or disregarding any claim limitation.' This provision would serve to buttress the underlying presumption in favor of eligibility. Unfortunately, in the wake of the *Alice* and *Mayo* decisions, and the Federal Circuit decisions that attempt to apply *Alice* and *Mayo*, too often courts have eliminated all the existing concrete limitations of a claim in a piecemeal fashion, rather than considering the claimed subject matter as whole, with the ultimate effect being to render the claimed invention ineligible."[6]

Still further, prominent Federal Circuit judges have remarked on the issue. For instance, Judge Linn lamented on the structural problems of the Federal Circuit's misapplication of the *Alice/Mayo* test and the regular abuse of the "as a whole" issue when determining patent eligibility. *Smart Systems Int'l v. Chicago Transit*, 873 F.3d 1364 (Fed. Cir. 2017).

Petitioner is not asserting that *Alice/Mayo* is inconsistent with this Court's other precedent. Petitioner is merely asserting that, unless this Court makes desperately-needed clarification, the USPTO and lower courts will continue to abuse the patent eligibility test developed by this Court. Unless and

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[6] https://www.judiciary.senate.gov/download/partridge-testimony at p. 3

until the USPTO and lower courts adhere to the Supreme Court's "as a whole" requirement while addressing claim limitations with some cognizable analysis based in law and/or based in fact consistent with *Markman* and *Graham*, step 2 of the *Alice/Mayo* test will remain an inconsistent and confused exercise.

VI. Plea to Hold the *Bhagat* Petition in Abeyance

Petitioner does not require oral argument. Petitioner respectfully requests that, at worst, this case be held in abeyance pending the disposition of the underlying issue common to *Berkheimer* and *Vanda Pharmaceuticals.*

VII. Conclusion

If step 2 of the *Alice/Mayo* test is an issue of fact based on a comparison of the prior art at the time of the patent, Petitioner Bhagat's claims are clearly patent eligible. If certiorari is warranted for *Berkheimer* and *Vanda Pharmaceuticals*, it is respectfully asserted that certiorari is warranted for *Bhagat*. Certiorari is further warranted in light of the evidence and issues recently brought to prominence by the United States Senate signaling that the lower courts do not address limitations as a whole under the *Alice/Mayo* test as an issue of policy.

/s/ Burman Y. Mathis
Burman Y. Mathis

Attorney for Petitioner

Certification of Counsel

Present Counsel hereby certifies that this petition for rehearing is presented in good faith and not for delay. Present counsel also certifies that the grounds for this petition for rehearing are properly restricted under Supreme Court Rule 44 based on intervening circumstances in the form of recent Senate hearings as well as recently-published proposed language to reform Title 35 U.S.C. § 101 based on problematic behavior of the United States Patent and Trademark Office (USPTO) and the lower courts. Present counsel still further certifies that the grounds for this petition for rehearing are properly restricted to present a substantially narrow issue not previously presented to this Court that is identical to the single, narrow issue presented in *Hewlett Packard, Inc. v. Berkheimer*, Case No. 18-415.

/s/ Burman Y. Mathis

Burman Y. Mathis

Attorney for Petitioners

ANNEX R:

US Patents for Humanity Application, November 8, 2015

OMB 0651-0066 Approved for use through 8/31/15.
U.S. Patent and Trademark Office; U. S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Humanitarian Use Application

Application Title: **Pre-formulated lipids, tailored lipids, and balanced lipids and micronutrients**.

Application Date: November 8, 2015

Category: Nutrition

Organization Applying:

Primary Location of the applicants:

City: Palo Alto State: CA Country: USA

Public Contact Info:

Name:	Asha Nutrition Sciences, Inc.
Address:	PO Box 1000, Palo Alto, CA 94302
Email:	admin@asha-nutrition.com
Phone Number:	650-322-7861
Preferred contact method:	admin@asha-nutrition.com
Press contact:	admin@asha-nutrition.com

If you wish to provide private contact info to be notified about your application status, please email it to patentsforhumanity@uspto.gov. Otherwise we will use any contact info associated with your submission.

Qualifying Patents

1. List the relevant U.S. utility patents or patent applications you own or license that you wish to apply under. These patents must relate to the technology described in this submission. Add more rows if needed. Only one patent or patent application is required for eligibility. If any patents or applications are found ineligible, the remaining items will be considered. If no eligible items remain, the PTO may contact the applicants to determine if eligible material can be identified.

U.S. Patent Application Number (PCT Number) (PCT Publication number)	Title	Filing Date
12/426,034 (PCT/US2009/041114) (WO2009/131939 A9)	Lipid-Containing Compositions And Methods Of Use Thereof	April 17, 2009
13/332,251 (PCT/US2009/041114) (WO2009/131939 A9)	Lipid-Containing Compositions And Methods Of Use Thereof Allowed as of 17 December 2018	December 20, 2011
13/877,847 (PCT/US2011/056463) (WO 2012/051591 A2)	Optimized Nutritional Formulations, Methods For Selection Of Tailored Diets Therefrom, And Methods Of Use Thereof	April 4, 2013

2. Are any of these patents or patent applications licensed from an entity not listed as an applicant on this form?

   NO

In no more than five pages, please address the following questions.

Eligibility Questions

3. What humanitarian issue(s) does this application cover? If not widely recognized, provide enough information to determine whether the issues significantly affect the health or quality of life of an impoverished population.

This application covers, pre-formulated lipids, tailored lipids, and balanced lipids and micronutrients, a game-changing solution for protecting and advancing public health at foundational level, whereby millions of people worldwide can benefit particularly the impoverished populations.

The foundation to health is nutrition. The most important and difficult to manage nutrients consumed are lipids, which include omega-6, omega-3, and several antioxidants and phytochemicals. Micronutrients include antioxidants, phytochemicals, and minerals, which affect metabolism of omega-6, omega-3, and other fatty acids. Most of the chronic diseases are associated with mismanaged lipid consumption, further immunity and daily well being is affected by lipid consumption, furthermore lipid requirements are different for different members of the family (by body size, hormones…)(See *Bhagat et al. 2015, Arch Med Sci 2015; 11, 4: 807–818)*. In 2012, in the US chronic diseases affected 117 million people costing ~$2 trillion (http://www.cdc.gov/chronicdisease/overview/index.htm); worldwide chronic and infectious diseases affected ~2 billion people (http://www.who.int/healthinfo/global_burden_disease/estimates/en/index2.html).

Natural lipid sources, oils, nuts and seeds etc, are variable and unreliable in lipid content and composition, and they contain many components that materially affect lipid metabolism. Important lipids such as polyphenols and several phytochemicals are poorly understood and absent from available dietary guidance, see Dietary Guidelines for Americans (*http://www.cnpp.usda.gov/sites/default/files/dietary_guidelines_for_americans/ PolicyDoc.pdf*). Adding to the complexity is mass confusion in the field with many spins on what is desirable and what is not. For example, many bodies and publications have disparaged omega-6 or taught low amounts of omega-6 and low omega-6 to omega-3 ratios *(Lands, Nutrition Reviews 1986:44-6:189-95; Lands, Ann. N.Y. Acad. Sci. 1055: 179–192 (2005); Simopoulos, Ann Nutr Metab 1999;43:127–130; Hamazaki et al. World Rev Nutr Diet. Basel, Karger, 2003:92:109–132*), even though omega-6 is the most critical fatty acid for health. Further, too many supplements are sold without regard for interactions. For example, it is a misconception that omega-3, antioxidants, and phytochemicals are always good for health. Such issues have increased the risk of some diseases. It is extremely complex for public to solve this problem. For example, **less than 1%** of Americans can correctly name types of fats (see surveys at http://www.foodinsight.org), let alone lipids. Unless corrected, the chaotic out-of-context touting of nutrients will create further problems in the field of nutrition and consequently health.

Fatty acid composition of some common edible fats and oils.

Percent by weight of total fatty acids.

Oil or Fat	Unsat./Sat. ratio	Saturated					Mono unsaturated	Poly unsaturated	
		Capric Acid C10:0	Lauric Acid C12:0	Myristic Acid C14:0	Palmitic Acid C16:0	Stearic Acid C18:0	Oleic Acid C18:1	Linoleic Acid (ω6) C18:2	Alpha Linolenic Acid (ω3) C18:3
Almond Oil	9.7	-	-	-	7	2	69	17	-
Beef Tallow	0.9	-	-	3	24	19	43	3	1
Butterfat (cow)	0.5	3	3	11	27	12	29	2	1
Butterfat (goat)	0.5	7	3	9	25	12	27	3	1
Butterfat (human)	1.0	2	5	8	25	8	35	9	1
Canola Oil	15.7	-	-	-	4	2	62	22	10
Cocoa Butter	0.6	-	-	-	25	38	32	3	-
Cod Liver Oil	2.9	-	-	8	17	-	22	5	-
Coconut Oil	0.1	6	47	18	9	3	6	2	-
Corn Oil (Maize Oil)	6.7	-	-	-	11	2	28	58	1
Cottonseed Oil	2.8	-	-	1	22	3	19	54	1
Flaxseed Oil	9.0	-	-	-	3	7	21	16	53
Grape seed Oil	7.3	-	-	-	8	4	15	73	-

Also see *http://www.ars-grin.gov/duke/* for other lipid content.

Pre-formulated lipids, tailored lipids, or balanced lipids and micronutrient delivery to public, can prevent or at least reduce the suffering from many chronic diseases. Such pre-formulated lipids are particularly indispensable for impoverished populations who have inadequate access to medical care, are subjected to poor living conditions, and have poor knowledge to choose lipids making them disproportionately susceptible to infections and diseases. Thus, delivering pre-formulated lipids, tailored lipids, or balanced lipids and micronutrient to public, especially to impoverished populations, can significantly reduce incidence and/or severity of disease.

4. What technologies does this application cover? Provide a brief description of each and indicate how they relate to the patents or patent applications in question 1.

Technologies covered; product name: **LIPILIFE** (subject to change):

- US 12/426,034 and 13/332,251 cover **pre-formulated lipids** containing omega-6 and omega-3 with omega-6 to omega-3 ratios greater than 4:1 or omega-6 greater than 20% of total lipids, wherein their dosages are controlled and/or content of other lipids in controlled. These applications also cover **tailored lipids** delivery wherein ratios and/or amounts of omega-6 and omega-3 are controlled by age, gender, and diet type, and lipid-free or low-lipid foods are designed to complement the tailored lipids.
- US 13/877,847, covers **nutritional managements systems,** which include multi-component nutritional formulations and methods of providing nutrition by demographic cohorts, designed to control the delivery of lipids including omega-6 and micronutrients, including antioxidants and phytochemicals. It also covers computer systems by means of which public can be remotely guided to managing sensitive lipid and phytochemical consumption.
- It is important to manage the dosage of omega-6 and omega-3, and lipids that affect their metabolism, as discussed above. Many variables modulate the metabolism of various fatty acids. It is difficult for consumers to calibrate on a daily basis the demands of the body for various fatty acids, since the requirements of various biologically active unsaturated fatty acids change depending on age, gender, and various life style factors. It is possible that there could exist differences in the requirements of various fatty acids and their co-factors even among members of the same family. (*Bhagat et al. 2 015 Supra, page 808*)

5. What populations are your actions described in this application targeting? Please describe how these populations are impoverished, and how they are affected by the humanitarian issues described in question 4.

The patent applications (see appendices) describe that technologies covered have prophylactic and therapeutic effect on almost all medical conditions, such as menopause, musculoskeletal disorders, mood, cognitive function, neural disorders, mental disorders, obesity, diabetes, endocrine disorders, digestive system disorders, reproductive disorders, pulmonary disorders, renal diseases, ophthalmologic disorders, dermatological disorders, sleep disorders, dental diseases, cancer, infectious diseases, inflammatory diseases, and cardiovascular disease. Further, the described technologies improve quality of life by stabilizing hormones, mood, and sleep for example.

The actions described in this application are beneficial to all populations, particularly to impoverished populations who are disproportionately affected by infections and diseases and they have inadequate access to medical care.

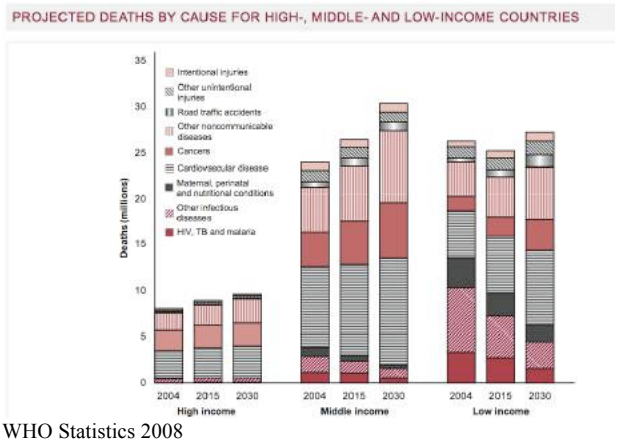
Chronic Health Problems Among U.S. Adults, by Poverty Status -- 2011

Poverty status is based on Gallup's best estimate of those in poverty according to the U.S. Census Bureau's 2011 thresholds

	In poverty	Not in poverty	Difference (pct. pts.)
% Depression	30.9	15.8	15.1
% Asthma	17.1	11.0	6.1
% Obesity	31.8	26.0	5.8
% Diabetes	14.8	10.1	4.7
% High blood pressure	31.8	29.1	2.7
% Heart attack	5.8	3.8	2.0
% Cancer	6.3	7.1	-0.8
% High cholesterol	25.0	26.0	-1.0

Jan. 2-Dec. 31, 2011
Gallup-Healthways Well-Being Index

GALLUP



WHO Statistics 2008

Thus, the disclosed solutions can especially reduce the burden of disease for impoverished populations. Applicant is targeting to provide the disclosed solutions in all economies with large share of impoverished populations.

Scoring Questions

6. Effectiveness – How do the applicants' technologies effectively address the humanitarian issues in question 5? Are any products or services that employ these technologies being used to benefit the target population?

Applicant's technologies effectively address almost all chronic and infectious diseases, which lead to ill health in 117 million people (133 million by some estimates) in US, and in ~2 billion people worldwide (http://www.who.int/healthinfo/global_burden_disease/estimates/en/index2.html). In fact, suffering is more than accounted here. For example, ~80% of females above the age of 13 (not counted in 2 billion) suffer from hormonal fluctuations, which can be debilitating and can be abated with controlled lipid delivery (*Filho et al., Reproductive Health 2011, 8:2*).

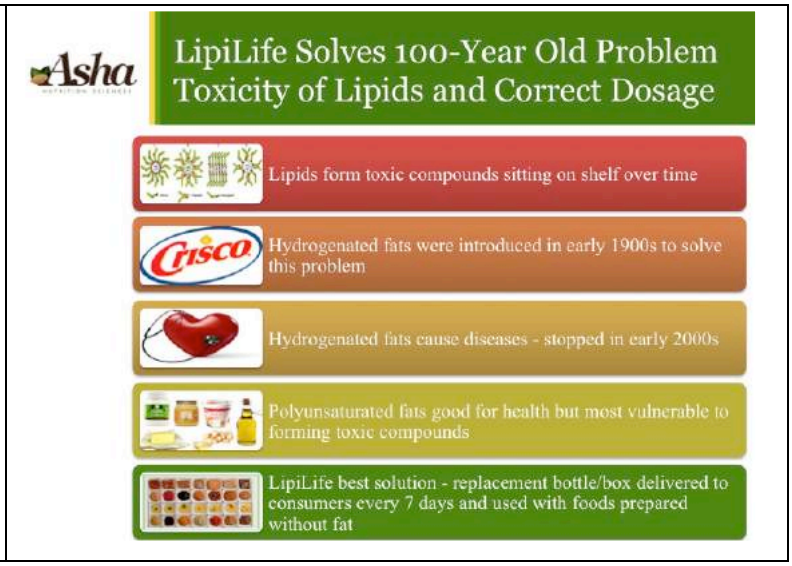
Most tissue contains ~10 times omega-6 as compared omega-3 and utilization of omega-6 is higher than omega-3. Omega-6 and other lipids are critical for optimal functioning of the cells and organisms (see *Bhagat et al, 2015* and *Morse 2009*). Further, immunity is materially enhanced by controlled lipid delivery. Therefore, health effects of the technology are at a broad level. Consumer feedback to LipiLife from preliminary market research has been positive (see table below). Several scientific publications published after the patent applications were filed, also report similar benefits from higher omega-6 consumption. See Appendices.

Thus, significant reduction in the cost of chronic diseases and human suffering can be achieved by implementation of the solutions disclosed in the patent applications. Some of the suffering and cost estimates are as follows:

United States Estimates (http://www.cdc.gov/chronicdisease/overview/)	Worldwide 2012 Estimates (http://www.who.int/healthinfo/global_burden_disease/estimates/en/index2.html)
• 86% percent of all health care spending, ~$2 trillion annual healthcare spending (2010) • ~117 million people affected by chronic diseases (2012)	• ~2 billion people suffer from chronic and infectious diseases • Heart disease and stroke ~393 million people • Cancer ~223 million people

• Costs of heart disease and stroke $315.4 billion (2010) • Costs of cancer care $157 billion (2010) • Costs of diagnosed diabetes $245 billion (2012) • Costs of arthritis and related conditions $128 billion (2003) • Costs linked to obesity $147 billion (2008)	• Diabetes ~60 million people • Musculoskeletal disorders ~111 million people • Infectious diseases ~432 million people • Neurological conditions ~80 million people

Additionally, LipiLife solves 100-year old problem of spoilage of unsaturated fats. In the 1900s, hydrogenated fats were introduced to solve the problem that unsaturated fats form toxic compounds sitting on shelf. However, we now know that hydrogenated fats are deleterious. We also know that unsaturated fats are critical for health, but cannot be added to food meant sit on shelf. The most effective solution is to pre-formulate and tailor lipids and deliver separately from the rest of the food, such that they are not made to sit on shelf for long durations, as LipiLife does. LipiLife is prepared separately from rest of the food and delivered in containers that are meant to last 1-4 weeks, i.e. not designed to sit on shelf for months.



The product, LipiLife, is in limited supply at present due to limited capital. Significant capital is necessary to effectively solve this problem, which includes public education in addition to product implementation. It is important for the patents to be granted for the Applicant to raise sufficient capital. All of the three applications are currently pending. Faster advancement of these applications is necessary for the applicant to secure sufficient capital and implement the solutions with public education to benefit the target populations.

7. Contribution – What meaningful actions did the applicants take to make the technology more available for addressing humanitarian issues?

Applicant is a small entity with very limited resources. Proprietors of the company have invested their personal intellectual and material resources for 10 years with dedication, without remuneration, to advance and implement the technology. Applicant needs sufficient capital to effectively solve this problem and patents need be granted to raise sufficient capital and effectively implement the solutions.

Applicant has committed to providing subsidized/free products to impoverished populations from part of the income generated from for-profit segments. Applicant plans to direct 10-25% of profits generated for providing subsidized/free products to impoverished populations. Such plans will be opportunistically revaluated based on Applicant's financial strength. Partnerships will be developed with governments and non-government organizations to collaborate on subsidized/free product distribution to impoverished populations. For example, Applicant has had

discussions for establishing such relationships with the following organizations: The HSC Foundation, The California Endowment, and California Wellness Foundation.

Applicant has invested very significant resources in building worldwide intellectual property portfolio in order to successfully make technology available to impoverished populations in economies with a disproportionate share of impoverished populations, such as Nigeria, Mexico, South Africa, Ukraine, Indonesia, Sri Lanka, China, and India.

8. Impact – How has deployment of the technology to benefit the target populations been significantly advanced as a result of the applicants' contributions? Are the target populations using the technology or products and services based on it? Are they benefitting in other ways? Include downstream actions by third parties stemming from the applicants' contributions.

As stated above, Applicant is a small entity. The products are currently in limited supply due to scarce resources. Applicant has put all resources available to deployment of the technology to benefit the target populations. Applicant has committed to providing subsidized/free products to impoverished populations from part of the for-profit segments returns, and to developing partnerships with governments and non-government organizations to collaborate on subsidized/free product distribution to impoverished populations. As evidenced throughout this application unprecedented humanitarian benefits can be realized through this technology.

> In the enclosed declarations from Drs. Rustagi, Rucker, and Das, the scientists declared:
>
> *"Thus, the art recognized in 1929 that the problem existed as noted in paragraph [0019]. However, the art has failed to solve the long-felt, critical and unmet need until the April 2008 priority date of the subject patent application, i.e. for ~80 years. There have been many persistent attempts as evidenced by the references cited above (e.g. Mark et al., whfoods.com, Lands 1986 and 2005; Simopoulos 1999; Hamazaki et al., 2003 supra), but the problem has not been solved. Lipid art has been struggling to find what are the right combinations of omega-6 and omega-3 and other lipids for consumption, how to keep the fatty acids stable on shelf (without formation of toxic compounds) but bio-available in-vivo (Chen and Chaiyasit supra). Inventions of instant claims 65, 91, 98, 122, 129, and 130 have devised the solutions. Thus, the invention of the subject patent application solves a long-felt critical persistent unmet need, and has great potential to protect and improve public health."* See para [0019]-[0023].
>
> *"[The technologies]… are well-reasoned and directed at much needed lipid solutions, particularly in light of mass erroneous teachings and confusion in the lipid art."* See para [0026]."

Thus, the technology has many immediate and long-term benefits.

- The immediate benefits are reduction in global disease burden and public suffering.
- Long-term benefits include solution to the problem of toxicity from spoilage of unsaturated fatty acids, which has plagued the society for over 100 years.
- Long-term benefits also include that tailored delivery of lipids and micronutrients can prevent diseases from acculturation because of tailoring to demographics.
- The disclosed approach will largely re-align the currently dysfunctional nutrition system.
- The technology has additional long-term benefits, such as when tailored lipids and micronutrients solve the large part of the disease burden, resources and research are focused on solving deeper causes of diseases in populations free of the confounding effects of mismanaged lipid consumption.

Thus, there are numerous immediate and downstream beneficial actions by third parties stemming from the applicants' contributions, which will advance humanitarian causes and make a lasting impact on humanity.

Additional Information

If there's any additional information you would like the judges to consider, include it here. Judges are not required to read more than five pages of material, not counting the pages of this form.

Appendices:

1. Bhagat et al. 2015, "Potential role of dietary lipids in the prophylaxis of some clinical conditions" Arch Med Sci 2015; 11, 4: 807–818
2. Lands, "Renewed Questions about Polyunsaturated Fatty Acids" Nutrition Reviews 1986:44-6:189-95
3. Lands, "Dietary Fat and Health: The Evidence and the Politics of Prevention" Ann. N.Y. Acad. Sci. 1055: 179–192 (2005)
4. Simopoulos, "Essentiality of and Recommended Dietary Intakes for Omega-6 and Omega-3 Fatty Acids" Ann Nutr Metab 1999;43:127–130
5. Calder PC, "Polyunsaturated fatty acids and inflammatory processes: New twists in an old tale" Biochimie 91 (2009) 791–795
6. Johnson et al., "Effect of Dietary Linoleic Acid on Markers of Inflammation in Healthy Persons: A Systematic Review of Randomized Controlled Trials" J Acad Nutr Diet. 2012;112:1029-1041.
7. Baum et al., Journal of Clinical Lipidology 2012:6:216–234 "Fatty acids in cardiovascular health and disease: A comprehensive update"
8. Morse. "A meta-analysis of blood fatty acids in people with learning disorders with particular interest in arachidonic acid" Prostaglandins, Leukotrienes and Essential Fatty Acids 2009:81:373–389
9. Lu et al. "Linoleic acid suppresses colorectal cancer cell growth by inducing oxidant stress and mitochondrial dysfunction" Lipids in Health and Disease 2010, 9:106.
10. Brasky et al., "Plasma Phospholipid Fatty Acids and Prostate Cancer Risk in the SELECT Trial" July 2010
11. Yip et al., "The Omega-3 Fatty Acid Eicosapentaenoic Acid Accelerates Disease Progression in a Model of Amyotrophic Lateral Sclerosis" PLoS ONE 8(4)
12. Declaration from Dr. Pradeep K. Rustagi dated September 29, 2014.
13. Declaration from Dr. Undurti N. Das dated September 30, 2014.
14. Declaration from Dr. Robert B. Rucker dated September 29, 2014.
15. Lipid-Containing Compositions And Methods Of Use Thereof
16. Optimized Nutritional Formulations, Methods For Selection Of Tailored Diets Therefrom, And Methods Of Use Thereof
17. Filho et al. "Essential fatty acids for premenstrual syndrome and their effect on prolactin and total cholesterol levels: a randomized, double blind, placebo-controlled study" Reproductive Health 2011, 8:2

ANNEX S:

Kent L. Erickson Testimony, October 7, 2012

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:	
Urvashi Bhagat	Examiner: West, Theodore R.
Application No. 12/426,034	Art Unit: 1628
Filed: April 17, 2009	Confirmation No. 3947
For: LIPID-CONTAINING COMPOSITIONS AND METHODS OF USE THEREOF	

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Kent L. Erickson, hereby declare:

[001] I received a Ph.D. in Anatomy from Oregon Health and Sciences University, Portland, OR, and I performed post-doctoral work at Oregon Regional Primate Research Center in the field of Dermatology. I served at a Scientist in the Cancer Metastasis and Treatment Laboratory at the National Cancer Research Institute, National Institutes of Health, Frederick, MD. I also served as a Researcher at the National Institute of Arthritis, Musculoskeletal and Skin Diseases of the National Institutes of Health, Bethesda, MD. I was an Underwood Fellow of the Biotechnology and Biological Sciences Council-UK and worked in the Centre for Stem Cell Biology at the University of Sheffield, UK. I served as Chair of the Department of Cell Biology & Human Anatomy at the University of California, Davis, School of Medicine for 17 years. Since 1975, I have been employed by The University of California, Davis, School of Medicine, where I currently hold the position of Professor.

[002] I am not an inventor, applicant, owner, or assignee of the above-referenced patent application. I serve on the Scientific Advisory Board (SAB) of Asha Nutrition Sciences, the assignee of the subject application. I have been allotted a modest amount of stock option grant

as compensation for my SAB role. I have not received any compensation specifically for preparing this declaration. I have read the above-referenced patent application.

[003] Prior to April 2008, the scientific knowledge of the polyunsaturated fatty acid (PUFA) was that high amounts of ω-6 PUFAs were unhealthy for humans and animals. This misconception began as early as 1974, when Silver injected sodium arachidonate into the marginal ear veins of rabbits (Silver *et al*., *Science* 1974, 183:1085-1087). Those investigators hypothesized that because the ω-6 PUFA, arachidonic acid (AA), caused platelet-aggregation in human plasma *in vitro*, it may also induce platelet aggregation *in vivo*. To test this hypothesis, rabbits were injected with 0.5, 0.7, 1, 1.4 or 6 mg/kg AA. All animals injected with 1.4 or 6 mg/kg AA died within 3 minutes. Three of the 12 animals injected with lower concentrations also died rapidly; 5 others exhibited rapid respiration. Five animals that survived initial doses of AA were later challenged with 1.4 mg/kg; all died within 2 minutes. Pathological examination of lung tissues from all animals killed by AA revealed that platelet aggregates had occluded the pulmonary microcirculation, whereas the tissues of control animals did not show the same platelet aggregation or occlusion. Those investigators concluded that AA triggered platelet aggregation *in vivo*. Such aggregation could lead to thrombotic diseases such as pulmonary embolism, myocardial infarction, and stroke.

[004] Other researchers also concluded that ω-6 PUFAs were linked to the pathogenesis of diseases such as pulmonary embolism, myocardial infarction, and stroke. In 1986, Lands, (*Nutrition Reviews*, 44:189-195) reviewed the biochemical characteristics of PUFAs, particularly the characteristics that make some PUFAs essential in the human diet. Although AA is essential, he reported that too much AA could be dangerous. For example, in addition to the Silver study, Lands reported that 6 grams of AA daily caused an increased thrombotic tendency in healthy volunteers. Increased amounts of another ω-6 PUFA, linoleic acid (LA), were reported to cause an increase in tumors. Specifically, the development of DMBA (7,12-dimethylbenz(a)anthracene)-induced rat mammary tumors increased step-wise with increasing LA levels up to 4.4% by weight of the diet (Ip *et al.*, *Cancer Res.* 1985, 45:1997-2001). These reports led Lands to conclude that "supra-optimal amounts of *n*-6 essential fatty acids could promote pathophysiology."

[005] Simopolous (*Am. J. Clin. Nut*. 1991, 54:438-63) reviewed the role of fatty acids, particularly ω-3 PUFAs, in health, disease, growth and development. Simopolous reported that

the amount of ω-6 PUFAs in the human diet has significantly increased over time, and that the increased amounts of ingested ω-6 PUFAs increase the production of AA-derived eicosanoids. According to Simopolous, "eicosanoids from AA are biologically active in very small quantities and if they are formed in large amounts they contribute to the formation of thrombus and atheroma; to allergic and inflammatory disorders; and to proliferation of cells." Thus, Simopolous concluded, "a diet rich in ω-6 fatty acids shifts the physiological state to one that is prothrombotic and proaggregatory with increases in blood viscosity, vasospasm, and vasoconstriction and decreases in bleeding time."

[006] In contrast to the negative effects caused by ω-6 PUFAs, early research had suggested that ω-3 PUFAs provided health benefits, including suppressing the pathogenesis of the same diseases that high ω-6 fatty acid levels were believed to promote (See, *e.g.*, Simopolous, p. 444-453). Thus, previous recommendations were for the consumption of diets with low amounts of ω-6 PUFAs as well as a low ω-6 to ω-3 fatty acid ratio in order to promote human and animal health.

[007] Simopolous' review favorably cited a 1990 scientific report from the Canadian Government, Ministry of Health that low amounts of ω-6 PUFAs for both sexes and all age groups except for pregnant and lactating women. The Canadian government recommended a maximum of 10 and 7 grams of ω-6 per day for adult males and females, respectively; a maximum of 11 and 7 grams of ω-6 per day for teenage males and females, respectively; and a maximum of 8 and 7 grams of ω-6 per day for school-age males and females, respectively.

[008] This early body of research failed to fully appreciate many factors important to the overall picture of dietary fatty acids' roles in health and disease. For example, researchers now know that results obtained from injecting animals with fatty acids cannot be translated to effects of oral administration of fatty acids. Early researchers also did not take into account factors such as absolute amounts of ω-6, ω-3, or total fat, or antioxidant and phytochemical contents in diets. As researchers performed more, and more comprehensive, studies, a more complete picture of fatty acids' role in human and animal health developed. Consequently, the state of the art shifted and the recommended daily dietary intake of ω-6 PUFAs increased. The art now generally views high amounts of ω-6 PUFAs as beneficial to human and animal health.

[009] The American Heart Association, a non-profit industry leader in cardiac care, has issued a scientific advisory that exemplifies the presently accepted view in the art (Harris *et al.*,

Circulation 2009, 119:902-907). The AHA reviewed extensive evidence on the relationship between ω-6 PUFAs and coronary heart disease (CHD) and cardiovascular disease (CVD) from more than 50 randomized trials, case-control and cohort studies, and long-term animal feeding experiments. Study results demonstrated that LA blood/tissue content, even at very high (i.e. >12% of energy) levels, was inversely associated with CHD risk. AA levels were not related to CHD risk. Other studies demonstrated that an increased LA intake, from 2.8% to 7.0%, decreased CHD risk by 25%. Evidence from randomized trials in humans showed reduced CHD risk with ω-6 intakes of 11-21% of energy for up to 11 years with no indications of harmful effects. Based on the aggregate data, the AHA came to the conclusion that "an omega-6 PUFA intake of at least 5% to 10% of energy," which is more than the art had often previously recommend, is beneficial to human health.

[0010] Czernichow *et al.*, (*Br. J. Nutrition* 2010, 104:788-796) also reviewed evidence on the relationship between ω-6 PUFAs and cardiovascular disease risk factors. That group cited evidence that ω-6 PUFAs decrease blood pressure. They cited studies that showed a negative correlation between LA content of adipose tissue and both systolic and diastolic blood pressure. An increase in plasma levels of LA was also associated with a decrease in both systolic and diastolic blood pressure. Decreased blood pressure correlates with a reduced risk of CVD.

[0011] In addition, Czernichow's review report ω-6 PUFAs were not associated with elevated levels of inflammatory markers. Higher plasma levels of ω-6 were associated with lower levels of serum pro-inflammatory markers. They also cited another study which reported that dietary supplementation with ω-6 PUFAs had no significant effect on inflammatory cell numbers or neutrophil and monocyte responses.

[0012] Czernichow believes that the body of evidence on ω-6 PUFAs demonstrates that they do not increase other CVD risk factors such as thrombus susceptibility, oxidative stress, or obesity. Based on the review of evidence on the relationship between ω-6 PUFAs and CVD risk factors, they concluded that the "body of data supports the recommendation for *n*-6 PUFA intake above 5%, and ideally about 10% of total energy". This conclusion reflects the present state of the art.

[0013] Russo, (*Biochem. Pharmacol* (2009, 77:937-946) reviewed PUFAs, essential fatty acids, and their role in cardiovascular diseases. Russo acknowledged that earlier studies about the role of ω-6 PUFAs in cardiovascular disease had been "controversial," but

demonstrated that overall, most studies do not reach the conclusion that elevated tissues AA and LA are detrimental with respect to cardiovascular risk. Specifically, a review of studies investigating the association between fatty acid composition and CVD risk suggested that lower LA content was associated with an increased risk for non-fatal events. Thus, decreasing LA, was detrimental.

[0014] Several groups have established that ω-6 PUFAs were not associated with an increase in cholesterol, which is a risk factor for CVD. Choo *et al.* (*Am. J. Clin. Nutr*. 2010 91:1195-203) analyzed serum fatty acids and measured serum particle concentrations for three subclasses each of VLDL, LDL, and HDL in a population-based study of 1098 men. Across all populations, serum LA was significantly and inversely associated with large VLDL, total LDL, and small LDL particle concentrations. Serum LA was significantly and positively associated with large HDL particle concentrations. Serum AA was significantly and inversely associated with large VLDL particle concentration, and significantly and positively associated with large HDL particle concentration. Because particle concentration of LDL is reported to be a risk factor for CVD, the inverse association of LA with total LDL suggests that LA reduces CVD risk. Because large HDL particle concentration may be associated with a reduced risk of carotid atherosclerosis, coronary progression, and cardiovascular events, the positive association of LA and AA with large HDL further suggests that LA and AA reduce CVD risk. Thus, Choo demonstrated that the ω-6 PUFAs LA and AA may reduce CVD risk through reduction in CVD-associated serum lipoproteins.

[0015] Czernichow reported that ω-6 PUFAs significantly lower blood LDL-cholesterol levels. For example, when the dietary proportion of saturated fatty acids (SFA) remained constant and ω-6 fatty acids replaced carbohydrates, a decrease in plasma levels of LDL cholesterol was observed. For a 1% replacement of carbohydrates with ω-6 PUFAs, the plasma LDL level decreased by 0.02 mmol/L. Replacing dietary SFA with ω-6 PUFAs also decreased plasma cholesterol concentration. Replacing 5% of energy from SFA with ω-6 PUFAs led to a 0.39 mmol/L decrease in total blood cholesterol. The total cholesterol:HDL-cholesterol (C) ratio, which is considered a better predictor of CVD than HDL alone, also decreased when the percentage of plasma ω-6 PUFAs increased. Czernichow's review concludes that "replacing SFA by *n*-6 PUFA . . . . lead to a substantial reduction in total and LDL-C cholesterol, as well as a reduction of the total cholesterol:HDL-C ratio, and may reduce the risk of CVD."

[0016] Several groups have disproven the previously held belief that ω-6 PUFAs are always pro-inflammatory. Calder (*Biochimie* 2009, 91:791-795) presented a summary of the links between the ω-6 PUFA AA and inflammation. AA is metabolized into eicosanoids, a family of inflammatory mediators that includes prostaglandin E_2 (PGE_2). PGE_2 is a potent inhibitor of two inflammatory cytokines, tumor necrosis factor (TNF)-α and interleukin (IL)-1. PGE_2 also leads to the decreased production of some pro-inflammatory leukotrienes and increased production of anti-inflammatory lipoxins. Thus, although PGE_2 may also have pro-inflammatory effects, "some AA-derived eicosanoids may be very important in . . . turning off inflammation."

[0017] Fritsche (*Prostagland. Leukot. Essent. Fatty Acids* 2008, 79:173-17) reviewed data from studies on the link between dietary ω-6 PUFA intake and inflammation in humans. He found that the evidence "fails to show a link between higher dietary LA intake . . . and greater inflammation . . . . In fact, some of the data suggest the opposite, i.e. higher dietary LA reduces inflammation." . In one of the reviewed studies, subjects with the lowest quartile of plasma ω-6 had the highest levels of the pro-inflammatory markers TNFα and IL-6, and the lowest levels of the anti-inflammatory markers IL-10 and TGF-β. Subjects with the highest quartile of plasma AA had the lowest levels of IL-6 and the highest levels of TGF- β. Plasma LA alone was not correlated with any inflammatory markers. In a separate study, high intakes of ω-6 were associated with the lowest levels of inflammation. In another study, the addition of 1200 mg of dietary AA per day for up to 7 weeks had no effect on the production of pro-inflammatory cytokines. Thus, higher ω-6 was not shown to increase inflammation.

[0018] Fritsche attributed the previous misconception about ω-6's role in inflammation to a "failure to fully appreciate the essential role that AA-derived lipid mediators play in resolving inflammatory responses in vivo." Like Calder, Fritsche showed that the accumulated data "clearly indicate AA serves as a precursor for a group of potent anti-inflammatory mediators" and that both "LA and AA metabolites play a significant role in reducing inflammation."

[0019] Based on the reviewed studies, Fritsche also found that "[calls for reducing the current dietary recommendations for LA intake . . . are not supported by the existing data." Thus, when Fritsche began his abstract with the statement, "Controversy exists over how much linoleic acid (LA) should be consumed in a healthy diet," he was merely putting his review into historical context. After analyzing studies on the link between dietary ω-6 PUFA intake and

inflammation in humans, he clearly concluded that "within the ranges of intake that are achievable for most human populations, the evidence do not support reducing LA intake below current consumption levels."

[0020] Most investigators in the field now believe that the total amounts of ω-6, ω-3, and total fat are important considerations when making recommendations about dietary intake of fatty acids. Russo reviewed the biochemistry and metabolism of PUFAs generally and essential fatty acids specifically, as well as their roles in cardiovascular diseases. Russo concluded that dietary recommendations regarding ω-3 PUFAs should also "strongly consider[], at the individual level, the intake of total energy, total fats and *n*-6 FA intake." p. 944.

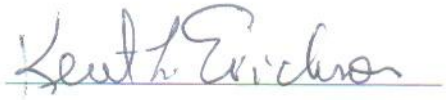
[0021] The Canadian Ministry of Health, which in 1990 had recommended low amounts of ω-6 PUFAs in the diet, now recommends higher amounts for both sexes and all age groups (Health Canada, Dietary Reference Intakes, updated Nov. 2010, http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb-dgpsa/pdf/nutrition/dri_tables-eng.pdf). In 1990, the Canadian government's highest recommendation for daily ω-6 intake was 11 grams, and that was only for 16-18 year-old males. Today the government recommends 11 grams or more ω-6 for males of all age groups starting at 9 years of age and females of all ages groups starting at 14 years old. Further, the highest recommendation for daily ω-6 intake is now 17 grams for males aged 19-50 years, which represents a greater than 50% increase in the recommended amount. The government has similarly increased the recommended amounts of ω-6 for every other sex and age group. These recommendations reflect how dietary PUFA recommendations have changed over time.

[0022] In my opinion, as one who has published for the past 25 years in the field of polyunsaturated fatty acid, the position taken in the subject application reflects the current state of the art. The subject application recognizes that the unpredictable results of early research in this field were incomplete and incorrect due to a failure to account for one or more factors that influence fatty acid metabolism. When the more recent and comprehensive research is taken into account, it is clear that a high amounts of ω-6 PUFAs are not detrimental to human or animal health. Instead, as in the subject application, a high amount of ω-6 PUFAs for optimal human and animal health reflects the state of the knowledge in the field.

[0023] The subject application contains very important focal points that were not understood prior to this disclosure. Most important of those as discussed above is that the prior

understanding failed to fully appreciate the importance of omega-6 for health. Human and animal tissues and organs contain many times the amount of omega-6 as compared to omega-3. Omega-3 can be preferentially metabolized. However, omega-6 has a shorter in-vivo life, possibly due to myriad of critical metabolites for which it is a precursor. Therefore, a lot more omega-6 is usually required as compared to omega-3. This disclosure indicates that deficiency of omega-6 is a greater problem. The disclosure focuses on the fact that certain nutrients, including antioxidants and phytochemicals can effectively enhance omega-3 bioactivity in-vivo but inhibit the metabolism of omega-6. The risks of sudden increase of omega-6 or withdrawal of omega-3 have been explained, which was not previously appreciated or incorporated into dietary strategy. Prior dogma held that omega-6 causes disease, whereas this disclosure explains that the deficiency of omega-6 potentiates certain mechanisms, such that sudden increases in omega-6 have an overflow effect which can lead to myocardial infarction, strokes, infections, and physiological disturbances. Several examples have been given to manage menopause, sleep disorders, neural disease, mental function, musculoskeletal disorders, obesity, diabetes, digestive, reproductive, pulmonary, ophthalmologic, dermatologic, and immune functions. These are multiple significant discoveries. Novel methods of treatment, administration, use, and tailored preparation are also disclosed. Because omega-6 and omega-3 significantly impact the structure and function of multiple physiological processes, correct delivery has a beneficial effect on many diseases. Sufficient directions are provided for the practitioner in the disclosure.

[0024] I further declare that all statements made herein of my own knowledge are true and that statements made of information and belief are believed to be true. I further acknowledge that any willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001, and may jeopardize the validity of the application or any patent issuing therefrom.



Date: 7 October 2012

Kent L. Erickson

4852-7980-7505\1

ANNEX T:

Kent L. Erickson Testimony, January 31, 2014

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:	
Urvashi Bhagat	Examiner: West, Theodore R.
Application No. 12/426,034	Art Unit: 1628
Filed: April 17, 2009	Confirmation No. 3947
For: LIPID-CONTAINING COMPOSITIONS AND METHODS OF USE THEREOF	

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Kent L. Erickson, hereby declare:

[001] I received a Ph.D. in Anatomy from Oregon Health and Sciences University, Portland, OR, and I performed post-doctoral work at Oregon Regional Primate Research Center in the field of Dermatology. I served as a Scientist in the Cancer Metastasis and Treatment Laboratory at the National Cancer Research Institute, National Institutes of Health, Frederick, MD. I also served as a Researcher at the National Institute of Arthritis, Musculoskeletal and Skin Diseases of the National Institutes of Health, Bethesda, MD. I was an Underwood Fellow of the Biotechnology and Biological Sciences Council-UK and worked in the Centre for Stem Cell Biology at the University of Sheffield, UK. I served as Chair of the Department of Cell Biology & Human Anatomy at the University of California, Davis, School of Medicine for 17 years. I also served as a member of the editorial board of the Journal of Nutrition for 4 years; the American Journal of Clinical Nutrition for 6 years and the Journal of Food Science and Nutrition

for 16 years. From 1975 to 2013, I was employed as a professor by The University of California, Davis, School of Medicine; I currently hold the position of Professor and Chairman Emeritus.

[002] I am not an inventor, applicant, owner, or assignee of the above-referenced patent application. I serve on the Scientific Advisory Board (SAB) of Asha Nutrition Sciences, the assignee of the subject application. I have been allotted a modest amount of stock option grant as compensation for my SAB role. I have not received any compensation specifically for preparing this declaration. I have read the above-referenced patent application. I have also read the Office Action issued by the Office dated January 21, 2014, and the references cited by the Examiner in the Office Action.

[003] It is obvious from the instant patent application that composition and formulation claims are directed to man-made product formulations, and not products of nature. For example note "combination" in para 29, 44, 66, 69, 73, "three or more" in para 11, and "incorporation of nuts and nut oils as integral components of formulations" in para 21. Additionally, the claims of the subject patent are directed to dosage and concentrations of omega-6 and omega-3 in relation to other lipids. However, products of nature do not come with guidance on omega-6 dosage amount or predictable concentrations of any of the lipids. Lipid content, including omega-6 and omega-3, of products of nature is extremely variable. This variability depends on the source, background genetics, cultivating conditions, including soils, fertilizer used, and other variable factors, such as hours of sunlight and water composition inherent in the cultivation of plant crops and many other epigenetic factors.

[004] Examiner has alleged that from US Patent No. 5,549,905 by Mark et al., a person skilled in the art would view the disclosure of reference to a one-liter composition as a representative quantity. However, as skilled in the art, by reading Mark et al., I do not conclude that one-liter composition is disclosed as the representative quantity of the total amount provided to the pediatric patient. Lipid composition is provided on a wt% of total fatty acids basis and rest of the data are provided for energy concentration. Although it is not stated in the reference, one assumes that it is gross energy not metabolizable or net energy. The dosage of Mark et al. compositions to be provided to the patient has not been stated specifically but could be a few milliliters to several liters. Mark et al., simply disclose a concentration of omega-6 in the composition, but not the upper or safe limit of omega-6 dosage. Additionally, one could consider an actual specific dosage or a range of values disclosed by Mark et al., if a reference

was given for an actual data point or range of omega-6 dosages. There is no actual data point or value for the maximum dosage or any dosage of omega-6 disclosed by Mark et al.

[005] Examiner has alleged that US Patent No. 5,635,199 by Trimbo et al., discloses a pediatric nutritional composition, in which one liter contains 22.7 grams of omega-6 fatty acid, therefore it discloses an omega-6 dosage. However, as skilled in the art, by reading Trimbo et al., I do not believe that Trimbo et al disclose omega-6 dosage or upper limit. The dosage of Trimbo et al. to be provided to the patient is not given; the volume to be given and the basis for it's the recommendation such as by body weight of BMI has not been provided. Thus, the amount of Trimbo et al. compositions administered to the patient could be a few milliliters to several liters. Trimbo et al., simply disclose a concentration of omega-6 in the composition, but not the upper limit of omega-6 that could be provided. There is no actual data for the maximum dosage or any dosage of omega-6 disclosed by Trimbo et al. In fact, in claim 23, Trimbo et al suggests administration of at least one liter of the composition, without any upper limit teaching. Thus, Trimbo et al disclose no upper limit of omega-6 dosage.

[006] Examiner has alleged that US Patent No. 5,635,199 by Trimbo et al., discloses a product known as PEDIASURE, which has an omega-6 to omega-3 ratio of 9:1 and contains 49.7g of fat per 1000 calories, 50% (24.85g) of which is safflower oil, and 30% is soy oil, anticipates claim 65(2) of the subject patent application in view of Anonymous, cited by the Examiner. Since the specific gravity of PEDIASURE has not been provided one cannot check the calculations because lipid is given by weight and rest of the calculation is based on energy. One assumes that the kilo Joules values have been based on gross energy not actual measured values. However, the amount of omega-6 in the PEDIASURE composition not calculated or measured by Trimbo et al. cannot be estimated, because of variability in lipid content of products of nature. Furthermore, even if amount of omega-6 can be estimated per 1000 calories of PEDIASURE, this is not the disclosure of dosage of omega-6 being no more than 40g. The dosage of PEDIASURE could be a few milliliters to several liters. Thus, the upper limit of omega-6 dosage in PEDIASURE cannot be estimated from Trimbo et al. and Anonymous taken together. There is no mention of PEDIASURE dosage or omega-6 dosage by Trimbo et al.

[007] I further declare that all statements made herein of my own knowledge are true and that statements made of information and belief are believed to be true. I further acknowledge that any willful false statements and the like so made are punishable by fine or

imprisonment, or both, under 18 U.S.C. §1001, and may jeopardize the validity of the application or any patent issuing therefrom

Kent Erickson Date: 1/31/2014

Kent L. Erickson

4852-7980-7505\1

ANNEX U:

Pradip K. Rustagi Testimony, September 29, 2014

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:	
Urvashi Bhagat	Examiner: Heyer, Dennis.
Application No. 12/426,034	Art Unit: 1628
Filed: April 17, 2009	Confirmation No. 3947
For: LIPID-CONTAINING COMPOSITIONS AND METHODS OF USE THEREOF	

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Pradip K. Rustagi, hereby declare:

[001] I received a M.D. from The Ohio State University, had clinical training in internal medicine, and performed post-doctoral work at Duke University and the State University of New York at Buffalo in the fields of hematology and oncology. I was a Scientist at the University of Alabama at Birmingham Comprehensive Cancer Center and Co-Head of the Section of Laboratory Hematology and Hemostasis at UAB Hospital. My research was concerned with biochemical aspects of cellular function. I am currently in the private practice of internal medicine, hematology, and oncology, directly involved in preventive care and health maintenance and in the nutritional and dietary needs of patients with a variety of medical conditions. Since 1998, I have also been employed by Lucile Packard Children's Hospital at Stanford, where I currently hold the position of Adjunct Clinical Associate Professor of

Medicine (Hematology) in the Departments of Medicine and Pediatrics of the Stanford University School of Medicine.

[002] I am not an inventor, applicant, owner, or assignee of the above-referenced patent application, nor am I otherwise affiliated with the subject application. I have not received compensation, financial or otherwise, for preparing this declaration. I have read the above-referenced patent application. I have also read all the other documents references in this declaration.

[003] I interact with many professionals in my career who possess ordinary skills in the art, such as doctors, scientists, nurses, dieticians, nutritionists, and the like ("skilled artisans"). These professionals typically have advanced degrees such as masters, Ph.Ds., and/or M.Ds. I am closely aware of the knowledge and skill levels of such professionals. I am confident in declaring that the following matters are clear to me and would be clear to other skilled artisans.

[004] The independent claims 65 and 91 of the subject patent application are recited below. Claim 129 is the same as claim 65(1) and claim 130 is the same as claim 65(2) but with additional elements.

> Claim 65. A lipid-containing formulation comprising a man-made mixture of different products, the mixture including at least a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater; wherein
>
> (1) the fatty acids comprise omega-6 fatty acids at 4-75% by weight of total lipids and omega-3 fatty acids at 0.1-30% by weight of total lipids; or
>
> (2) omega-6 fatty acids are not more than 40 grams.

> Claim 91. A lipid-containing formulation comprising a man-made mixture of different products, including at least polyunsaturated, monounsaturated, and saturated fatty acids, wherein omega-6 fatty acids are greater than 20% by weight of the total lipids, wherein the formulation includes at least
>
> (i) one or more polyunsaturated fatty acids selected from..., and
>
> (ii) nutrients including at least
>
> (a) one or more polyphenols, or
>
> (b) one or more phytochemicals,
>
> the one or more phytochemicals being selected from: phytosterols, campesterol, sitosterol, stigmasterol, organosulfur, sulfide, melatonin, lycopene, lutein, zeaxanthin, and a phenol.

[005] US Patent No. 5,549,905 by Mark et al. column 4, lines 40-60 disclose 12.2% C18:2 n6, which is linoleic acid (LA) one of the omega-6 fatty acids, and 2.4% C18:3 n3, which is alpha-linolenic acid (ALA) one of the omega-3 fatty acids. Further, amount of linoleic acid 4.7g, and alpha-linolenic acid 0.9g is disclosed. Mark et al. do not disclose concentrations of total omega-6 and/or total omega-3 fatty acids as a weight of total lipids or amount of total omega-6 or total omega-3 fatty acids used in the formulations anywhere in the disclosure. The concentration or amount of total omega-6 or total omega-3 fatty acids cannot be calculated from the table in column 4 because only 86% of the fatty acids and 33.1g of the 38.5g lipids are disclosed; 14% of the fatty acids and 5.4g of the lipids are missing. Furthermore, column 2, lines 24-26, of Mark et al. teach a composition having an "omega-3 to omega-6 fatty acid ratio of approximately 4:1 to 6:1" or omega-6 to omega-3 of 1:4 to 1:6, and this teaching is repeated in column 2 lines 37-39. Inconsistent teaching in column 2, 4, and 6 and missing lipids in column 4 make it impossible to determine what is being taught. Further, Mark et al. do not count lipid vitamins and phytochemicals in lipids as evidenced by recitation of ingredients in column 5, lines 57-62, which groups oils and fats separately as lipids, without including lipid vitamins and phytochemicals in the same group. This erroneous grouping is also evident from Mark et al.'s table in column 4 where fatty acids are recited without lipid vitamins and phytochemicals, even though the heading of the table recites "LIPID PROFILE (38.5 g/L)." The lipid vitamins and phytochemicals are recited separately in the table in column 6, lines 17-21, which add up to less than 0.1g, therefore cannot be a significant part of the missing 5.4g of lipids. Thus due to inconsistencies in ratio teachings, incomplete information in table in column 4, and erroneous grouping of lipids, I find that Mark et al. is not a credible reference, and that the practitioner using Mark et al. will not know how much omega-6 or omega-3 to put into the formulations of columns 4 and 6. Another US Patent 5,635,199 by the same inventor "David A. Mark" has the same errors and inconsistencies. Both US Patent No. 5,549,905 and 5,635,199 are not credible references for these reasons. Thus, I do not believe that US Patent No. 5,549,905 and 5,635,199 disclose all elements of instant claims recited in paragraph [004].

[006] The webpages at www.whfoods.com list 130 foods considered healthy by the site at (http://web.archive.org/web/20061230052716/http://www.whfoods.com/foodstoc.php). Each of the 130 foods has a dedicated main page where opinions held by the site regarding Health Benefits, Description, History, How to Select and Store, How to Enjoy, Safety, and Nutritional Profile for the food are disclosed. Each of the 130 foods also has an associated page titled "In depth nutrient analysis." In order to disclose nutrient concentrations in the foods, the website chooses an "amount" for each food, such as 0.25 cup, 1 cup, or 1 tablespoon. However, these amounts are not logical serving amounts for all of the foods. For example, 1.00 cup of olives is not logical serving amount for olives, 0.25 cup is not a logical serving amount for sesame seeds, and 2.00 teaspoons of cloves is not a logical serving amount for cloves. These foods would be excessive and inedible in such amounts for most people, and can also have adverse health effects. Conventionally, these foods are consumed in much smaller amounts, for example, a pinch ($1/16^{th}$ of a teaspoon) of cloves due to its strong phytochemical content is considered sufficient for two servings (http://www.whfoods.com/genpage.php?tname =recipe&dbid=242). Consequently, I do not believe that the "amounts" disclosed are "servings," they are simply a measure for disclosing concentrations of nutrients.

[007] Olives, walnuts, soybeans, and sunflower seeds are four of the 130 foods listed on the site. Main pages for these foods are as follows:

"Olives" (published December 31, 2006)
http://web.archive.org/web/20061231072745/http://www.whfoods.com/genpage.php?tname=foodspice&dbid=46
"Walnuts" (published December 12, 2006)
http://web.archive.org/web/20061212181741/http://www.whfoods.com/genpage.php?tname=foodspice&dbid=99
"Soybeans" (published December 31, 2006)
http://web.archive.org/web/20061231072929/http://www.whfoods.com/genpage.php?tname=foodspice&dbid=79
"Sunflower Seeds" (published December 31, 2006)
http://web.archive.org/web/20061231072831/http://www.whfoods.com/genpage.php?tname=foodspice&dbid=57

"In-depth nutrient analysis" pages for these foods are as follows:
"ONA" Olives Nutritional Analysis (published December 31, 2006)
http://web.archive.org/web/20061231074543/http://www.whfoods.com/genpage.php?tname=nutrientprofile&dbid=111
"WNA" Walnuts Nutritional Analysis (published December 31, 2006)

http://web.archive.org/web/20061231074659/http://www.whfoods.com/genpage.php?tname=nutrientprofile&dbid=132

"SBNA" Soybeans Nutritional Analysis (published November 9, 2006)

http://web.archive.org/web/20061109220456/http://www.whfoods.com/genpage.php?tname=nutrientprofile&dbid=17

"SSNA" Sunflower Seeds Nutritional Analysis (published November 9, 2006)

http://web.archive.org/web/20061109215807/http://www.whfoods.com/genpage.php?tname=nutrientprofile&dbid=127

There is no suggestion in the reference for mixing of "Walnuts", "Soybeans", and "Sunflower Seeds."

[008] ONA, WNA, SBNA, and SSNA do not give a complete nutrient or lipid profile of olives, walnuts, soybeans, or sunflower seeds. ONA, WNA, SBNA, and SSNA appear to capture nutrients that whfoods.com considers relevant for its purpose. For example, olives are known to contain other lipids besides the lipids listed in ONA, e.g lutein zeaxanthin, phytosterols, and squalene but ONA does not list them. Walnuts are known to contain other lipids besides lipids listed in WNA, for example, phytosterols, and gamma- and delta-tocopherols, but WNA does not capture them. Other lipids known to be present in soybeans are not captured by SBNA, for example, saponins, phytosterols, and beta-, gamma- and delta-tocopherols. Other lipids known to be present in sunflower seeds are not captured by SSNA, for example, phytosterols, and gamma- and delta-tocopherols. Therefore, lipid profiles in ONA, WNA, SBNA, and SSNA are incomplete and incorrect. Following sites evidence presence of additional lipids in olives, walnuts, soybeans, and sunflower seeds: http://www.ars-grin.gov/duke/, http://en.wikipedia.org/wiki/Olive, and http://lpi.oregonstate.edu/infocenter/. Further, minor variations in lipid components in a formulation can make a major impact on physical and chemical properties of the formulation (*Chen et al., Critical Reviews in Food Science and Nutrition, 51:901–916 (2011)* and *Chaiyasit et al., Critical Reviews in Food Science and Nutrition, 47:299–317 (2007)*).

[009] There is no mention of "lipids" in ONA, WNA, SBNA, or SSNA and there is no mention or even a suggestion of omega-6 and/or omega-3 as a ratio of total lipids. Further, the references group nutrients in groups considered relevant for their purpose. The fact that ONA, WNA, SBNA, or SSNA group the lipid "Cholesterol" separately under the heading "Basic

Components", lipid vitamins separately under the heading "Vitamins", and lipid fatty acids "18:2 linoleic, 18:3 linolenic, 18:4 stearidon, 20:4 arachidon, 20:5 EPA, 22:5 DPA, and 22:6 DHA" separately under the heading "Poly Fats," and then add up the "omega 3 fatty acids" and "omega 6 fatty acids" is evidence that "Basic Components", "Vitamins", "Poly Fats", "omega 3 fatty acids", and "omega 6 fatty acids" are the categories that the references consider relevant. "Total Lipids" group is not considered relevant by the references; therefore the category does not appear. The categories "Total Lipids" and "omega-6 …by weight of total lipids" are not present in the references. There is nothing in the reference that suggests a category of "Total Lipids"; lipids are dispersed without any suggestion of them belonging to a group. Therefore, the practitioner is neither motivated nor taught to modify ONA, WNA, SBNA, or SSNA in order to obtain total lipids or a ratio of omega-6 and/or omega-3 to total lipids from the references.

[0010] The webpages at www.whfoods.com teach choosing and mixing of the 130 foods for "Eating Healthy." At page 9 of http://web.archive.org/web/20070104020351/http://whfoods.com/genpage.php?tname=faq&dbid=7 the reference teaches, "The ideal ratio of omega-3 to omega-6 is not known, but is estimated to be around 1:2; whereas, the current ratio in the typical American diet is more like 1:25. In order to achieve a more beneficial ratio, it is important to decrease the amount of omega-6 fatty acids in your diet, while increasing the amount of omega-3 fatty acids like EPA, DHA, and alpha-linolenic acid." Thus, the site unmistakably teaches mixing various foods such that overall ratio of omega-6 to omega-3 is around 2:1. This teaching is applicable to all food mixtures taught by the site including olives in oil or brine. Olives in oil or brine are part of the mixtures taught by the site to be mixed with other foods, wherein overall omega-6 to omega-3 ratio is around 2:1. The reference Olives specifically teaches mixing of olives with tuna/fish, which are known to contain high amounts of omega-3. Thus, Olives teaches use of olives in mixtures where omega-6 to omega-3 ratio is around 2:1.

[0011] Olives or ONA do not teach 1.00 cup of olives as a "serving." There is no mention of 1.00 cup of olives as "serving" in the webpages. The purpose of the recitation in Olives and ONA of "Amount" and/or "1.00 cup" is simply to disclose the concentration of

nutrients per cup of olives. The reference teaches random topping of olives on pasta, tuna, or chicken salad or as a plate of hors d'oeuvres in section titled "How to Enjoy." There is no mention of serving size or an amount to be administered in the reference specific to olives. The reference discloses a "Food Rating System Chart" for the purpose of showing the nutrients for which the food is either an excellent, very good or good source; and an associated "In depth nutrient analysis," which details nutrient content per an "amount." This is a generic methodology that the reference uses for all the foods. The reference discloses some food preparations for which "serving" is specified, such as "Nutrients in 15 minute Halibut With Avocado Salsa" and "Nutrients in Moroccan Eggplant With Garbanzo Beans." This constitutes evidence that 1.00 cup amount in olives is not a "serving" because the reference treats the disclosure differently. As skilled artisan I do not consider that Olives discloses 1.00 cup of olives as a serving.

[0012] The use of the word "dosage" in the subject patent application is clearly directed to determination of amount to be administered and/or administration in prescribed amounts (see para 34, 39, 47, 48, 49, 57, 59, 89, 97, 101, and 103). The concentration of nutrients per cup of olives in the reference fails to disclose such predetermined/ prescribed amount to quantify the olives for a person to eat.

[0013] Ratio of omega-6 to total lipids is neither present nor suggested in "Diamond Walnuts" in http://www.labelwatch.com/product_pop.php?id=1577 (published 2007), WNA, and "Corn Oil Nutritional Analysis" (CNA) in http://www.fda.gov/ohrms/dockets/dockets/06p0243/06p-0243-cp00001-059-APPENDIX-S1-NUTRIENT%20ANALYSISCORNOIL.pdf taken together. As noted above in paragraph [009], the categories "Total Lipids" and "omega-6 …by weight of total lipids" are neither present nor suggested in WNA. Similarly, CNA groups lipid vitamins separately under the heading "Vitamins" and carotenoid lipids separately under the heading "Other", but not under the heading "Lipids" where fatty acids and sterols are listed. The category "Total lipid (fat)" refers to fat, which is a subset of lipids. Thus, lipids are dispersed in different categories in CNA. Further, there is nothing in the reference that suggests a ratio of omega-6 fatty acids to total lipids. Therefore, the practitioner is neither motivated nor

taught to modify Diamond walnuts, WNA and CNA in order to obtain total lipids or a ratio of omega-6 to total lipids. Further, minor variations in lipid components in a formulation can make a major impact on physical and chemical properties of the formulation (see paragraph [008]).

[0014] The subject patent application has disclosed important factors that were neither conventional nor understood by the prior art regarding omega-6 and omega-3 fatty acids. Prior to April 2008, the state of the polyunsaturated fatty acid (PUFA) art had held that high amounts of omega-6 PUFAs were unhealthy for humans and animals. Numerous publications taught to keep omega-6 less than 4% of calories, (*Lands, Nutrition Reviews 1986:44-6:189-95; Simopoulos, Ann Nutr Metab 1999;43:127–130; Hamazaki et al. World Rev Nutr Diet. Basel, Karger, 2003:92:109–132*), which equals less than 11.4% of dietary fat (proxy for lipids) based on ~35% dietary calories from fat generally recommended *(USDA & USDHHS "Dietary Guidelines for Americans 2010"*). This teaching applied to omega-6 from all foods, including omega-6 from nuts and seeds. Therefore, prior art teaches omega-6 less than 11.4% of total dietary fat, including from combination of walnuts, soybeans and sunflower seeds. Furthermore, *Lands, Ann. N.Y. Acad. Sci. 1055: 179–192 (2005),* teaches, less than 0.5% of calories from omega-6, i.e. less than 1.42% of dietary fat based on 35% of dietary calories from fat (page 183, 4th paragraph). The teaching is specific to "a [average] day's menu," i.e. including walnuts, soybeans, and sunflower seeds. Lands discloses distance-learning sites hosted by US National Institutes of Health (http://web.archive.org/web/20051212173212/http://efaeducation.nih.gov/sig/kim.html), which "use the USDA data base of 6,000 different foods, more than 12,000 servings of food, to create an interactive, computerized, personalized, daily menu-planning program..." (page 188). It is well known that walnuts, soybeans, and sunflower seeds are part of the USDA database of foods (see http://www.nal.usda.gov/fnic/foodcomp). Thus, *Lands* teaches omega-6 less than 1.42% of total dietary fat, and "distance-learning sites" were developed to help users implement this teaching. Thus, the prior art overwhelmingly teaches omega-6 less than 11.4% of total fat including from walnuts, soybeans and sunflower seeds, which is outside the scope of instant claim 91. Thus, the limitation "omega-6 fatty acids are greater than 20% by weight of the total lipids," in claim 91 is neither well understood, nor conventional or routine in prior art, rather there is overwhelming opposite teaching in prior art.

[0015] The webpages at www.whfoods.com teach choosing and mixing of the 130 foods for "Eating Healthy." At page 9 of http://web.archive.org/web/20070104020351/http://whfoods.com/genpage.php?tname=faq&dbid=7 the reference teaches, "[i]t is important to decrease the amount of omega-6 fatty acids in your diet…" The reference "whfoods.com" **is disparaging and discrediting** mixtures of foods (including walnuts, soybeans, and sunflower seeds) that increase "the amount of omega-6 fatty acids in your diet." Skilled artisans would have interpreted this instruction to mean "keep omega-6 less than 11.4% of total fat including from walnuts, soybeans, and sunflower seeds" because of overwhelming such teachings in the art prior to April 2008, e.g. from Lands, Simopoulos, and Hamazaki. Therefore, www.whfoods.com teaches mixtures (including "Walnuts," "Soybeans," and "Sunflower Seeds", though the specific mixture is not taught by whfoods.com) that are opposite of claim 91, which teaches, "omega-6 fatty acids are greater than 20% by weight of the total lipids."

[0016] The subject patent application has disclosed unexpected results. It is noted in paragraph 6, 7, and elsewhere in the specifications. Several examples are given where omega-6 greater than 20% by weight of total lipids was administered (tables 15-17) and omega-6 greater than 11g was required to overcome adverse health (see examples 11, 12, 14.2, 17, 19, 26, and 27), i.e. at least 5.82% of calories (11g *9cal = 99 cal /1700 = 5.82%, see table 20) and 22% of lipids (11g linoleic acid /50g total lipids, see table 20). Example 11 is menopause case, 12 is CVD case, 14.2 is ALS case, 17 is obesity case, 19 is digestive health case, 26 is dental health case, and 27 is an immunity case. Thus, improved properties in multiple indications have been shown. Some of the examples provide more detail regarding the amounts of omega-6 and/or omega-3 administered than the other examples, but the examples are easily correlated. Even in the examples where amounts administered are not disclosed (such as examples 13, 16, 23, 24, and 25) useful additive information is disclosed. It is not necessary to repeat the amounts administered in every example. Omega-6 is a critical nutrient and is a crucial component of cell membranes, a precursor to critical biological messengers, and a regulator of cellular functions and genes; therefore delivery correction has beneficial effects on all indications. It is well known in the art that omega-6 levels influence many diseases and conditions including menopause,

cardiovascular diseases, mental disorders, neural disorders, musculoskeletal disorders, endocrine disorders, cancer, digestive system disorders, symptoms of aging, viral infections, bacterial infections, obesity, overweight, renal diseases, pulmonary disorders, ophthalmologic disorders, dermatological disorders, sleep disorders, dental diseases, and the diseases of the immune system including autoimmunity (see paragraph 6 of the application). Delivery of omega-6 in the correct amounts will therefore clearly have a positive effect on diseases and disorders that are influenced by fatty acid levels. The subject patent application teaches what that correct delivery is. Skilled artisans can easily correlate the results in various examples. Therefore, improved properties of omega-6 at above 20% by weight of total lipids in many indications have been disclosed, which is unexpected in light of prior art teachings discussed in paragraph [0014] and [0015] above. These unexpected results are commensurate in scope with the invention of claim 91. Further, publication published after the priority date of the subject patent application have demonstrated that there is no evidence that omega-6 are harmful at achievable levels (*Fritsche K. Prostaglandins, Leukotrienes and Essential Fatty Acids 79 (2008) 173–175* and *Johnson GH. J Acad Nutr Diet. 2012;112:1029-1041*). Furthermore, *USDA & USDHHS "Dietary Guidelines for Americans 2010" (Appendix 5, page 76)* recommends 5-10% of calories from linoleic acid (one of the omega-6 fatty acids) i.e. at least 20% of total fat based on ~35% of calories from fat.

[0017] As part of the correct fatty acid delivery teaching the following is clearly evident from the specifications:

a. Omega-6 to omega-3 ratio greater than 4:1 with the exception of low-antioxidant and low-phytochemical consumers (Tables 9, 10, 11, 14, 15, 16, 17, 18, original claim 4). Skilled artisans can easily obtain the definition of low-antioxidant and low-phytochemical consumer from paragraph 33 and rest of the disclosure.
b. Omega-6 greater than 20% by weight of total lipids (Table 15, 16, 17, 20, original claim 40).
c. Omega-6 dosage less than 40 grams (Tables 9, 10, 11, 12, 13).
d. Consider total lipids in formulating omega-6 and omega-3 delivery (Table 15, 16, 17, 20 and rest of the disclosure).
e. Limit monounsaturated fatty acids (Examples 12, 14.1, 15.2, 15.3, 20, and 22)
f. Antioxidants and phytochemicals will reduce the requirement/ tolerance for omega-3 and/or increase the requirement for omega-6 (paragraph 22 and rest of the disclosure).
g. Nuts, seeds, and nut oils have high antioxidants, mineral, and phytochemical content and other properties that can render excessive omega-3 unnecessary. Nuts and seeds have a narrow therapeutic window, unfavorable interactions, and other properties

requiring judicious use (paragraph 21, 30, 36).

h. Physiological disturbances may be experienced when omega-6 is increased and/or when omega-3 is decreased (see paragraph 39, 71, 73, 85, 95, 98).

i. Benefits can be achieved by tailoring daily amounts of fatty acids for a subject based on one or more factors selected from: age of the subject, sex of the subject, diet of the subject, the body weight of the subject, physical activity level of the subject, lipid tolerance of the subject, medical conditions of the subject, family medical history of the subject, and climate of the subject's living area (claims 98 and 122). The terms used are perfectly clear and standard terms in the art. Based on the specifications skilled artisans can tailor daily amounts of fatty acids based on the recited factors.

[0018] The unexpected results or improved properties reported by the subject patent application are also evident in comparison to individual foods considered "healthy," e.g. walnuts, soybeans, and/or sunflower seeds, which may naturally have omega-6 greater than 20% by weight of total lipids. The unexpected results/improved properties of claimed compositions reported by the subject patent application as compared to "Walnuts" considered "closest prior art" by the Office are as follows:

"Walnuts"	**Subject Patent Application**
¼ cup of walnuts provides 90.8%, i.e. 2.27g (see WNA) of the daily value for omega-3. Walnuts' concentration of omega-3s (a quarter-cup provides 90.8% of the daily value for these essential fats) has many potential health benefits ranging from cardiovascular protection, to the promotion of better cognitive function, to anti-inflammatory benefits helpful in asthma, rheumatoid arthritis, and inflammatory skin diseases such as eczema and psoriasis.	Example 12 reports very low levels of blood pressure at 1.8g of omega-3 daily (from oils nuts and seeds), and that blood pressure normalized at 1.2g of omega-3. Similarly, in example 19 Digestive Disorders, example 26 Dental Disorders, and example 27 Immunity and Inflammatory Diseases found ~1.2g omega-3 to be beneficial but higher amounts to be detrimental.
Walnuts Improve Cholesterol Profile in Persons with Type 2 Diabetes ¼ cup of "Walnuts" only contains 9.52g of omega-6.	Example 18 reports that reducing the dosage of omega-3 from high levels was found to reverse simulated symptoms of diabetes. The example further clarifies that the insulin resistance (in diabetes) can be due to low levels of omega-6. The "high" and "low" levels of omega-3 and omega-6 are easily interpreted by skilled artisans in light

	of the other examples where amounts are disclosed and 11-14.5g of omega-6 was found to be beneficial (e.g. examples 11, 12, 14.2, 17, 19, 26, and 27 and various tables).
Walnuts reduce levels of several molecules that promote atherosclerosis. "Walnuts" delivers 2.27g of omega-3 and 9.52g of omega-6 daily.	Example 12 reports 1.2g of omega-3 and 11g of omega-6 daily resulted in a reduction of LDL from 160mg to 120mg.
Hypes ellagic acid and antioxidants unconditionally	Paragraph 22 discloses that ellagic acid (in walnuts) and antioxidants in general, reduce the requirement/tolerance for omega-3. Nuts and seeds have high antioxidants, mineral, and phytochemical content and a narrow therapeutic window with unfavorable interactions and other properties requiring judicious use (paragraph 21, 30, 36). Paragraphs 79-80, 83, 102, and 103 report incidence of ALS, gout, dental disease, and compromised immunity, respectively, in context of nuts and seeds and higher omega-3 in the diet. The compositions disclosed use low amounts of walnuts: 2-33% in Table 5, 5-15% in paragraph 64, and 5-25% in paragraph 65 of the lipid formulations

In short "Walnuts" does not work because it delivers 2.27g of omega-3 daily from nuts and seeds, whereas example 12, 19, 26 and 27 of the subject patent application teach omega-3 less than 1.8g from nuts and seeds, preferably 1.2g daily; and "Walnuts" delivers 9.52g omega-6 daily, whereas examples 11, 12, 14.2, 17, 19, 26, and 27 of the subject patent application teach at least 11g omega-6 daily. "Walnuts" also fails to caution the practitioner about adverse effects of high nut consumption. Therefore, unexpected results and improved properties of claimed compositions have been reported by the subject patent application as compared to "Walnuts." Further, "Walnuts", Soybeans", and/or "Sunflower Seeds" from whfoods.com webpages do not teach someone skilled in the art, what mixture of walnuts, soybeans, and/or sunflower seeds to

use to arrive at the claimed mixtures. Therefore, skilled artisans will not have an expectation of success using "Walnuts", Soybeans", and/or "Sunflower Seeds."

[0019] The quest to find lipid formulations that lead to good health is a long-felt unmet need. *Holman, J. Nutr. 128: 427S–433S, 1998* explains, "The discovery of the essentiality of the long-chain fatty acids was made by Burr and Burr (1929) at the University of Minnesota Medical School. … At that time, essentiality meant growth and prevention of the dermatitis observed when a fat-free diet was fed to rats. Both linoleic and linolenic acids provided these functions." In 1960, Holman proposed an index of EFA deficiency status. In 1974, a misconception about omega-6 fatty acids began, which in part was based on inappropriate extrapolation about the effects of ingested omega-6 from data based on injected omega-6. For example, *Silver et al., Science (1974) 183:1085-1087,* injected sodium arachidonate into the marginal ear veins of rabbits, which caused death by platelet aggregate occlusion of the pulmonary microcirculation. Silver concluded that arachidonic acid (AA) was harmful to health because such aggregation could lead to thrombotic diseases such as pulmonary embolism, myocardial infarction, and stroke. However, contrary to the misunderstanding of the prior art, a given agent can have very different effects depending on its route of administration, and results from administration by one route—such as injection—cannot be equated to results from administration by another route—such as ingestion. Other researchers also concluded that omega-6 PUFAs were linked to the pathogenesis of diseases such as pulmonary embolism, myocardial infarction, and stroke. In contrast to the negative effects caused by omega-6 PUFAs, early research had suggested that ω-3 PUFAs provided health benefits, including suppressing the pathogenesis of the same diseases that high omega-6 fatty acid levels were believed to promote.

[0020] Accordingly, prior art overwhelmingly teaches to keep omega-6 consumption less than 11.4% of dietary fat as discussed in paragraph [0014], and prior art overwhelmingly teaches omega-6 to omega-3 ratios less than 4:1. For example, European Patent Application 1510133A1 teaches omega-6 to omega-3 ratio of 1:1; *Hulbert. Biol. Rev. (2005), 80, pp. 155–169* teaches omega-6 to omega-3 ratios closer to 1:1 and teaches against omega-6 to omega-3 ratios 16.67:1; Mustad et al., US Patent 7,759,507 B2 teaches omega-6 to omega-3 ratio 0.25:1-3:1 (abstract);

DeMichele et al., US5780451 teaches omega-6 to omega-3 ratio: 0.25-4.0 (Table 10); and www.whfoods.com teaches omega-6 to omega-3 ratio around 2:1 (see paragraph [0010]). This is a very small sample of such teachings.

[0021] Further, consistent with the widely-held belief that omega-6 is inflammatory and omega-3 is anti-inflammatory, in the prior art, when in-vitro and/or in-vivo omega-6 levels or the metabolites of omega-6 are found to be suppressed by certain nutrient(s) or omega-3 uptake or metabolism is enhanced by a certain nutrient(s), the nutrient(s) is(are) recommended as anti-inflammatory and its use is encouraged. For example, prior art has recommended use of vitamin E, curcumin, flavonoids, and other phytochemicals for suppression of PGE2 an arachidonic acid (omega-6) metabolite, assumed to be inflammatory, or inhibition of cycloxygenases (COX-1 and -2), enzymes responsible for formation of PGE2 (*Wu D. et al. Am J Physiol. 1998 Sep;275(3 Pt 1):C661-8*; *Shah et al., Biochemical Pharmacology, Vol. 58, pp. 1167–1172, 1999; O'Leary et al. Mutat Res. 2004 Jul 13;551(1-2):245-54*). Prior to the filing of the subject application, one of ordinary skill in the art would have thought that it was beneficial to suppress omega-6 activity (and the activity of cyclooxygenases). However, the current patent application teaches that long-term deficiency or suppression of omega-6 activity is harmful (see para 39, 71, 85, 95, 98). These findings have been validated by recent publications (e.g. *Calder Biochimie 91 (2009) 791–795* and *Andreasson K. Prostaglandins & other Lipid Mediators 91 (2010) 104–112.*

[0022] Furthermore, the prior art places emphasis on low omega-6 to omega-3 ratios without teaching amounts, and not on high ratios with upper limit on omega-6 amounts, as taught by subject patent application. As noted previously, Mark et al. neither teach a consistent ratio nor total omega-6 amounts. Without knowledge of the absolute values, the ratio has little meaning. To be of value, the ratio must be taught with amounts. Further, to be of value amounts of total omega-6 fatty acids have to be taught not just LA. This is a shortcoming in the art at large and there are significant gaps in the teaching.

[0023] Thus, the art recognized in 1929 that the problem existed as noted in paragraph [0019]. However, the art has failed to solve the long-felt, critical and unmet need until the April

2008 priority date of the subject patent application, i.e. for ~80 years. There have been many persistent attempts as evidenced by the references cited above (e.g. *Mark et al., whfoods.com, Lands 1986 and 2005; Simopoulos 1999; Hamazaki et al., 2003 supra*), but the problem has not been solved. Lipid art has been struggling to find what are the right combinations of omega-6 and omega-3 and other lipids for consumption, how to keep the fatty acids stable on shelf (without formation of toxic compounds) but bio-available in-vivo (*Chen and Chaiyasit supra*). Inventions of instant claims 65, 91, 98, 122, 129, and 130 have devised the solutions. Thus, the invention of the subject patent application solves a long-felt critical persistent unmet need, and has great potential to protect and improve public health.

[0024] The physical and chemical properties of "A lipid-containing formulation comprising a man-made mixture of different products" including omega-6 and/or omega-3 fatty acids is necessarily different from what occurs in nature because of at least the following reasons:

a. In nature, omega-6 and omega-3 occur in plant and animal tissue and organs primarily as part of triacylglycerols (TAG) (e.g. TAG constitute 89.6% of tallow and 97.9% of soybean oil) and in very small amounts as part of free fatty acids (e.g. 0.04% in rapeseed oil and 2.37% in sesame oil). The unsaturated fatty acids on triacylglycerols and phospholipids have low volatility. Free fatty acids are highly unstable causing odors, foaming, and reduced smoke points. Lipid sources that have been improperly stored can have high free fatty acid content.
b. In nature omega-6 and omega-3 occur along with several prooxidants (<3ppm), such as iron and copper, and antioxidants (<2%), such as phytosterols, tocopherols, and hydrocarbons. Prooxidants can accelerate lipid oxidation by directly interacting with unsaturated fatty acids to form lipid hydroperoxides (e.g. lipoxygenases and singlet oxygen) or by promoting formation of free radicals (e.g. transition metals or ultraviolet light promoted hydroperoxide decomposition). Antioxidants can retard lipid oxidation under certain conditions but promote lipid oxidation under other conditions.
c. Oxidation of omega-6 and omega-3 is one of the major causes of quality deterioration in lipid mixtures. The oxidation affects many physical and chemical characteristics such as flavor (rancidity), color, texture, and the nutritive value of mixtures. In addition, lipid oxidation produces and adds byproducts (e.g. aldehydes and ketones) to the mixture.
d. The only way to obtain "a man-made mixture of different products" comprising omega-6 and/or omega-3 fatty acids is to either mix plant/animal tissue itself or extract omega-6 and/or omega-3 fatty acids in free fatty acid form and then mix them. Either way the physical and chemical properties of the resulting mixture will be

significantly and markedly different from what occurs in nature because composition of triacylgycerols versus free fatty acids will change, and composition of prooxidants versus antioxidants will change. Additionally, triglyceride composition will change with respect to the type of fatty acids and the positional distribution of fatty acids (sn-position) on the glycerol backbone, affecting the physical and chemical properties.

e. Further, the physical properties of the mixture have a dramatic effect on lipid oxidation chemistry. For example dependent on whether the mixture is an oil-in-water emulsion, a bulk oil, or a mixture of another kind. Such mixtures contain polar lipids such as monoacylglycerols, diacylglycerols, free fatty acids, phospholipids, sterols, cholesterols, phenolic compounds, and oxidation by-products, many of which are amphiphlic. These amphiphilic molecules can self-assemble due to hydrophobic interaction from small amounts of water to form a variety of different types of association colloids, including lamellar structures and reverse micelles. These nano- or micro-environments can alter the physical location of prooxidants, antioxidants, and oxidation substrates (e.g. hydroperoxides).

(Chen et al., and Chaiyasit et al., supra)

It should also be kept in perspective that in nature there is extreme variability in lipid, antioxidant, and pro-oxidant content from species to species and even within species. Thus, hand of man in a "man-made mixture" will necessarily introduce variations to lipid configurations found in nature with major effect on physical and chemical properties of the lipid formulation. Thus, man-made lipid mixtures are necessarily different in physical and chemical properties from what occurs in nature.

[0025] In my opinion as a skilled practitioner in the art, the position taken in the subject application reflects the current state of the art. The subject application recognizes that the unpredictable results of early research in this field were incomplete and incorrect due to a failure to study long-term effects of higher omega-6 administration and to account for one or more factors that influence fatty acid metabolism. When the more recent and comprehensive research is taken into account as disclosed by the subject patent application, it is clear that omega-6 PUFAs above 20% by weight of total lipids are desirable, and omega-6 to omega-3 ratios of 4:1 or greater, wherein omega-6 are less than 40g, are desirable since human and animal tissue contains ~10x more long-chain omega-6 as compared to long-chain omega-3, and utilization of omega-6 is higher (*Morse. Prostaglandins, Leukotrienes and Essential Fatty Acids 2009:81:373–389*). Furthermore, as disclosed by subject patent application in general

phytochemicals and antioxidants increase requirement of omega-6 and reduce requirement/tolerance of omega-3 (also see *Thiebaut et al, Int. J. Cancer: 124, 924–931 (2009)*).

[0026] Thus, the limitations recited in independent claims 65, 91, 129 and 130 of the subject patent application are meaningful limitations. The limitations are not arbitrary. They are well-reasoned and directed at much needed lipid solutions, particularly in light of mass erroneous teachings and confusion in the lipid art. The subject patent application has disclosed upper limits of omega-6 throughout the disclosure, and a detailed example is disclosed in Table 20 along with calories administered. Using the information disclosed in various examples and rest of the disclosure, someone skilled in the art can formulate an omega-6 and/or omega-3 supplement or an entire nutritional formulation.

[0027] I further declare that all statements made herein of my own knowledge are true and that statements made of information and belief are believed to be true. I further acknowledge that any willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001, and may jeopardize the validity of the application or any patent issuing therefrom.

Date: September 29, 2014

Pradip K. Rustagi

4852-7980-7505\1

ANNEX V:

Robert B. Rucker Testimony, April 30, 2015

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:	
Urvashi Bhagat	Examiner: Heyer, Dennis.
Application No. 12/426,034	Art Unit: 1628
Filed: April 17, 2009	Confirmation No. 3947
For: LIPID-CONTAINING COMPOSITIONS AND METHODS OF USE THEREOF	

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Robert B. Rucker, hereby declare:

[001] I received a Ph.D. in Biochemistry from Purdue University, Lafayette, Indiana, and I performed post-doctoral work at the University of Missouri in the field of Nutritional Biochemistry and Metabolism. Since September 1970, I have been employed by the University of California - Davis campus, where I currently hold the position of Distinguished Emeritus Professor. During my tenure at University of California - Davis campus, I have served as Chair and Vice-Chair of the Nutrition Department and in various positions for the Graduate Group for Nutritional Sciences (cf. http://nutrition.ucdavis.edu/faculty/rucker/).

[002] I am not an inventor, applicant, owner, or assignee of the above-referenced patent application, nor am I otherwise affiliated with the subject application. I have not received compensation, financial or otherwise, for preparing this declaration. I have read the above-

referenced patent application. I have also read all the other documents referenced in this declaration.

[003] I interact with many professionals in my career who possess ordinary skills in the art, such as doctors, scientists, nurses, dieticians, nutritionists, and the like ("skilled artisans"). These professionals typically have advanced degrees such as masters, Ph.Ds., and/or M.Ds. I am closely aware of the knowledge and skill levels of such professionals. I am confident in declaring that the following matters are clear to me and would be clear to other skilled artisans. I have previously given a related declaration in favor of the subject patent application on September 29, 2014.

[004] The amended independent claims 65, 91, 129 and 130 of the subject patent application are recited below.

> 65. (Currently Amended) A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation, wherein at least one casing comprises an intermixture of lipids from different sources, and wherein
>
> (1) omega-6 fatty acids are 4-75% by weight of total lipids and omega-3 fatty acids are 0.1-30% by weight of total lipids; or
>
> (2) omega-6 fatty acids are not more than 40 grams.

> 91. (Currently Amended) A lipid-containing formulation, comprising a dosage of omega-6 fatty acids, wherein the omega-6 fatty acids are greater than 20% by weight of the total lipids, contained in one or more complementing casings providing controlled delivery of the formulation, wherein at least one casing comprises an intermixture of lipids from different sources, the formulation comprising polyunsaturated, monounsaturated, and saturated fatty acids, and wherein the formulation includes at least
>
> (i) one or more polyunsaturated fatty acids selected from linoleic acid (C18:2), conjugated-linoleic acid (C18:2), gamma-linolenic acid (C18:3), eicosadienoic acid (C20:2), di-homo-gamma-linolenic acid (C20:3), arachidonic acid (C20:4), alpha-linolenic acid (C18:3), stearidonic acid (C18:4), eicosapentaenoic acid (C20:5), docosapentaenoic acid (C22:5), and docosahexaenoic acid (C22:6), and
>
> (ii) nutrients including at least
>
> (a) one or more polyphenols, or
>
> (b) one or more phytochemicals,
>
> the one or more phytochemicals being selected from: phytosterols, campesterol, sitosterol, stigmasterol, organosulfur, sulfide, melatonin, lycopene, lutein, zeaxanthin, and a phenol.

> 129. (Currently Amended) A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation, wherein at least one casing comprises an intermixture of fatty acids from different sources, and wherein
>
> omega-6 fatty acids are 4-75% by weight of total lipids and omega-3 fatty acids are 0.1-30% by weight of total lipids.

130. (Currently Amended) A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation, wherein at least one casing comprises an intermixture of fatty acids from different sources, and wherein

omega-6 fatty acids are not more than 40 grams and the formulation further comprises one or more polyphenols, or one or more phytochemicals selected from: phytosterols, campesterol, sitosterol, stigmasterol, organosulfur, a sulfide, melatonin, lycopene, lutein, and zeaxanthin, or vitamin E-alpha/gamma less than 0.5% by weight of total lipids, or one or more specific protein types listed in Table 21 in a dosage not more than the upper limit disclosed in the table.

[005] In light of the specification of the subject patent application, "casing" or "one or more complementing casings providing controlled delivery of the formulation" in amended claims 65, 91, 129 and 130 means one or more casings that are designed to contain one or more dosages of the formulation in order to control the delivery (e.g., substantially avoid inadequate or excess delivery and/or substantially control the release). This is clear from, for example, paragraphs 10, 34, 37, 60, 61, and Tables 16-19 of the specification.

[006] In light of the specification of the subject patent application, "intermixture of lipids [fatty acids] from different sources" means a mixture, wherein at least fatty acids and/or other lipids are integrated from at least two "different sources" to enhance the usefulness of the formulation over a "single" source. "Different sources" means different oils, butters, nuts, seeds, herbs, sweeteners, and/or other foods and/or their different varieties (containing different lipid profiles). This is clear from, for example, paragraphs 8, 9, 11, 21, 22-27, 30, 62 and 64 and Table 2 of the specification.

[007] On September 29, 2014, I declared (see paragraph [0024]) that the physical and chemical properties of "A lipid-containing formulation comprising a man-made mixture of different products" including omega-6 and/or omega-3 fatty acids is necessarily different from what occurs in nature because of at least the reasons recited below. The same reasons hold true for "intermixture of lipids [fatty acids] from different sources" as opposed to a "single" source.

a. In nature, omega-6 and omega-3 occur in plant and animal tissue and organs primarily as part of triacylglycerols (TAG) (e.g. TAG constitute 89.6% of tallow and 97.9% of soybean oil) and in very small amounts as part of free fatty acids (e.g. 0.04% in rapeseed oil and 2.37% in sesame oil). The unsaturated fatty acids on triacylglycerols and phospholipids have low volatility. Free fatty acids are highly unstable causing odors, foaming, and reduced smoke points. Lipid sources that have been improperly stored can have high free fatty acid content.

b. In nature omega-6 and omega-3 occur along with several prooxidants (<3ppm), such as iron and copper, and antioxidants (<2%), such as phytosterols, tocopherols, and hydrocarbons. Prooxidants can accelerate lipid oxidation by directly interacting with unsaturated fatty acids to form lipid hydroperoxides (e.g. lipoxygenases and singlet oxygen) or by promoting formation of free radicals (e.g. transition metals or ultraviolet light promoted hydroperoxide decomposition). Antioxidants can retard lipid oxidation under certain conditions but promote lipid oxidation under other conditions.
c. Oxidation of omega-6 and omega-3 is one of the major causes of quality deterioration in lipid mixtures. The oxidation affects many physical and chemical characteristics such as flavor (rancidity), color, texture, and the nutritive value of mixtures. In addition, lipid oxidation produces and adds byproducts (e.g. aldehydes and ketones) to the mixture.
d. The only way to obtain "a man-made mixture of different products" comprising omega-6 and/or omega-3 fatty acids is to either mix plant/animal tissue itself or extract omega-6 and/or omega-3 fatty acids in free fatty acid form and then mix them. Either way the physical and chemical properties of the resulting mixture will be significantly and markedly different from what occurs in nature because composition of triacylgycerols versus free fatty acids will change, and composition of prooxidants versus antioxidants will change. Additionally, triglyceride composition will change with respect to the type of fatty acids and the positional distribution of fatty acids (sn- position) on the glycerol backbone, affecting the physical and chemical properties.
e. Further, the physical properties of the mixture have a dramatic effect on lipid oxidation chemistry. For example dependent on whether the mixture is an oil-in-water emulsion, a bulk oil, or a mixture of another kind. Such mixtures contain polar lipids such as monoacylglycerols, diacylglycerols, free fatty acids, phospholipids, sterols, cholesterols, phenolic compounds, and oxidation by-products, many of which are amphiphlic. These amphiphilic molecules can self-assemble due to hydrophobic interaction from small amounts of water to form a variety of different types of association colloids, including lamellar structures and reverse micelles. These nano- or micro-environments can alter the physical location of prooxidants, antioxidants, and oxidation substrates (e.g. hydroperoxides).

(Chen et al., and Chaiyasit et al., supra)

It should also be kept in perspective that in nature there is extreme variability in lipid, antioxidant, and pro-oxidant content from species to species and even within species. Thus, hand of man in a "man-made mixture" will necessarily introduce variations to lipid configurations found in nature with major effect on physical and chemical properties of the lipid formulation. Thus, man-made lipid mixtures are necessarily different in physical and chemical properties from what occurs in nature.

[008] Lipid sources, such as oils, butters, nuts, seeds, and herbs have 100s of compounds. Therefore, when lipids from different sources are intermixed, the resulting mixture will necessarily have different physical and chemical properties, as discussed above. A hypothetical mixture of lipids from Source A and lipids from Source B, where the resulting mixture has exactly the same properties as Source A or B is first practically impossible, and second, if possible, it would be an extremely complex scientific endeavor. There would be no motivation for a skilled artisan to intermix lipids from Source A and Source B to achieve exactly the same properties as Source A or Source B in the resulting formulation.

[009] It is a standard practice in the art to consider a food source, such as multiple walnuts (or olives) to be a single source (i.e., single type of source). In other words, each walnut

(or olive) would not be considered to be a different source of lipids from one another by skilled artisans, unless one specific variety of walnut (or olive) is added to another, different, specific variety of walnuts (or olives) to enhance usefulness of the walnut (or olive) formulation. A reference utilizing a mixture of different varieties of walnuts (olives) to enhance usefulness of the formulation would have to disclose that such a result is/was contemplated. A random mixture of single source foods, such as walnuts (or olives) would not be considered to be an "intermixture of lipids from different sources" by a skilled artisan. This simply would not be a reasonable interpretation by a skilled artisan.

[0010] On September 29, 2014, in reference to US Patent No. 5,549,905 by Mark et al., I declared as follows (see paragraph [005]):

> US Patent No. 5,549,905 by Mark et al. column 4, lines 40-60 disclose 12.2% C18:2 n6, which is linoleic acid (LA) one of the omega-6 fatty acids, and 2.4% C18:3 n3, which is alpha-linolenic acid (ALA) one of the omega-3 fatty acids. Further, amount of linoleic acid 4.7g, and alpha-linolenic acid 0.9g is disclosed. Mark et al. do not disclose concentrations of total omega-6 and/or total omega-3 fatty acids as a weight of total lipids or amount of total omega-6 or total omega-3 fatty acids used in the formulations anywhere in the disclosure. The concentration or amount of total omega-6 or total omega-3 fatty acids cannot be calculated from the table in column 4 because only 86% of the fatty acids and 33.1g of the 38.5g lipids are disclosed; 14% of the fatty acids and 5.4g of the lipids are missing. Furthermore, column 2, lines 24-26, of Mark et al. teach a composition having an "omega-3 to omega-6 fatty acid ratio of approximately 4:1 to 6:1" or omega-6 to omega-3 of 1:4 to 1:6, and this teaching is repeated in column 2 lines 37-39. Inconsistent teaching in column 2, 4, and 6 and missing lipids in column 4 make it impossible to determine what is being taught. Further, Mark et al. do not count lipid vitamins and phytochemicals in lipids as evidenced by recitation of ingredients in column 5, lines 57-62, which groups oils and fats separately as lipids, without including lipid vitamins and phytochemicals in the same group. This erroneous grouping is also evident from Mark et al.'s table in column 4 where fatty acids are recited without lipid vitamins and phytochemicals, even though the heading of the table recites "LIPID PROFILE (38.5 g/L)." The lipid vitamins and phytochemicals are recited separately in the table in column 6, lines 17-21, which add up to less than 0.1g, therefore cannot be a significant part of the missing 5.4g of lipids. Thus due to inconsistencies in ratio teachings, incomplete information in table in column 4, and erroneous grouping of lipids, I find that Mark et al. is not a credible reference, and that the practitioner using Mark et al. will not know how much omega-6 or omega-3 to put into the formulations of columns 4 and 6…

I further declare that Mark et al consistently discloses and claims omega-6 to omega-3 ratios in triglycerides, not in total lipids. This is evident from column 4 lines 21-23, which recite, "The lipid profile containing such long chain triglycerides is designed to have a polyunsaturated fatty acid omega-6 (n-6) to omega-3 (n-3) ratio of approximately 4:1 to 6:1." Further, a composition of triglycerides is the focus of entire Mark et al disclosure, for example see abstract, column 2 lines 9-11, 21-23, and 48-51, and column 4 lines 1-23, and all of the

independent claims 1, 9, and 15. Mark et al. claim 6 is a dependent claim on claim 1. The claim 1 and claim 6 in combination read as follows:

> An enteral composition designed for pediatric patients comprising:
> a hydrolyzed protein source comprising approximately 12% of the total calories;
> a carbohydrate source; and
> a lipid source comprising a mixture of medium and long chain triglycerides, wherein at least 55% of the lipid source are medium chain triglycerides [. The composition of claim 1] <u>further comprising</u> an omega-6 to omega-3 fatty acid ratio of approximately 4:1 to 6:1.

Thus, the Mark et al. omega-6 to omega-3 ratio claimed in claim 6 is also in fatty acids of triglycerides.

Triglycerides are a subset of total lipids. Total lipids are well-known by persons of ordinary skill in the art to include free fatty acids, mono-glycerides, di-glycerides, glycolipids, and phospholipids, which contribute fatty acids to total lipids. The lipid sources that Mark et al discloses (in column 2, 4, 5, and 6) safflower oil, canola oil, soy oil, coconut oil (MCT), residual milk fat, and soy lecithin are known to contain free fatty acids, mono-glycerides, di-glycerides, glycolipids, and phospholipids, which contain omega-6 and omega-3 fatty acids. Soy lecithin, for example, can contain ~90% glycolipids and phospholipids, and the soy lecithin phospholipids can be rich in omega-6 and omega-3 fatty acids. Thus, Mark et al entire disclosure discloses omega-6 to omega-3 fatty acid ratios in triglycerides only, and fails to count fatty acids from free fatty acids, mono-glycerides, di-glycerides, glycolipids, and phospholipids in its compositions and omega-6 to omega-3 ratios. This is the logical reason for why 14% of fatty acids and 5.4g of lipids are missing from the table in column 4 of Mark et al. It is practically impossible for non-fatty acid-containing lipids to add up to 5.4g in 38.5g of lipids in the kind of compositions disclosed by Mark et al. When omega-6 to omega-3 ratio is 4:1 to 6:1 in triglycerides, it can be 1:4 to 1:6 in total lipids, as recited in column 2 lines 24-26 and 37-38 of Mark et al. Thus, in my expert opinion, Mark et al has not disclosed omega-6 to omega-3 ratio of 4:1 or greater in total lipids as in instant claims 65, 129, and 130.

Therefore, as declared previously, Mark et al is not a credible reference. The reference uses terms such as “Total” and “lipids” negligently as in the table in column 4 and in column 5 last paragraph, and the reference fails to teach compositions with total omega-6 and omega-3 in total lipids, even though minor omega-6 and omega-3 constituents of free fatty acids, mono-

glycerides, di-glycerides, glycolipids, and phospholipids can have major impact on the properties of the formulation and health of subject consuming such formulations. A practitioner using Mark et al will not know what omega-6 to omega-3 ratios to use in total lipids and how much omega-6 and omega-3 to put into Mark et al formulations because of negligent use of terms, and the gaps and inconsistencies in the disclosure.

[0011] "Olives" is one of the ~130 foods listed on the site www.whfoods.com. The archived version of "Olives" (published March 14, 2006) is http://web.archive.org/web/20060314112112/http://www.whfoods.com/genpage.php?pfriendly=1&tname=foodspice&dbid=46. Olives In-depth Nutrient Analysis "ONA" (published March 14, 2006) is the associated page http://web.archive.org/web/20060314112106/http://www.whfoods.com/genpage.php?tname=nutrientprofile&dbid=111 disclosing nutrients in Olives. There is no suggestion in either Olives or ONA for "intermixture of lipids [fatty acids] from different sources," as recited in instant claims in paragraph [004]. As a skilled artisan, I consider one or more servings of olives to be a single source and I do not consider each olive to be a different source of lipids [fatty acids] from one another. Unless there is a specific, different type of olive added to the olives to enhance usefulness of the olives (as discussed above). There is no such suggestion of such a combination in either Olives or ONA.

[0012] "Walnuts" is one of the ~130 foods listed on the site www.whfoods.com. The archived version of "Walnuts" (published November 9, 2006) is http://web.archive.org/web/20061109221131/http://www.whfoods.com/genpage.php?pfriendly=1&tname=foodspice&dbid=99. Walnuts In-depth Nutrient Analysis "WNA" (published November 9, 2006) is associated page http://web.archive.org/web/20061109221127/http://www.whfoods.com/genpage.php?tname=nutrientprofile&dbid=132 disclosing nutrients in Walnuts. There is no suggestion in either Walnuts or WNA for "intermixture of lipids [fatty acids] from different sources" as recited in the instant claims and in paragraph [004]. As a skilled artisan, I consider one or more servings of walnuts to be a single source and I do not consider each walnut to be a different source of lipids from one another. Unless there is a specific, different type of walnut added to the walnuts to enhance usefulness of the walnuts (as discussed above). There is no such suggestion of such a combination in either Walnuts or WNA.

[0013] On September 29, 2014, in reference to whfoods.com disclosure, I declared that (see paragraph [009]):

> There is no mention of "lipids" in ONA, WNA… and there is no mention or even a suggestion of omega-6 and/or omega-3 as a ratio of total lipids. Further, the references group nutrients in groups considered relevant for their purpose. The fact that ONA, WNA, … group the lipid "Cholesterol" separately under the heading "Basic Components", lipid vitamins separately under the heading "Vitamins", and lipid fatty acids "18:2 linoleic, 18:3 linolenic, 18:4 stearidon, 20:4 arachidon, 20:5 EPA, 22:5 DPA, and 22:6 DHA" separately under the heading "Poly Fats," and then add up the "omega 3 fatty acids" and "omega 6 fatty acids" is evidence that "Basic Components", "Vitamins", "Poly Fats", "omega 3 fatty acids", and "omega 6 fatty acids" are the categories that the references consider relevant. "Total Lipids" group is not considered relevant by the references; therefore the category does not appear. The categories "Total Lipids" and "omega-6 …by weight of total lipids" are not present in the references. There is nothing in the reference that suggests a category of "Total Lipids"; lipids are dispersed without any suggestion of them belonging to a group. Therefore, the practitioner is neither motivated nor taught to modify ONA, WNA, … in order to obtain total lipids or a ratio of omega-6 and/or omega-3 to total lipids from the references.

The above form of disclosure is typical of almost all food nutrient databases. In this context it is important to note that the significance of "total lipids" as a category is not well understood in the art, even though the definition/classification of lipids is well known (see *The Nomenclature of Lipids, J Lipid Res. 1978 Jan;19(1):114-28*). The effect of minor lipid components, such as various phytochemicals in health and physical and chemical properties of formulations is not well understood. Food labeling practices routinely ignore important lipid components, as evidenced by Mark et al, ONA, WNA, and whfoods.com in general. Further, various authoritative nutrient databases (such as USDA databases) similarly disperse lipids over various categories and miss to report several important lipids and significance of "total lipids" as a category. Even authoritative guidelines do not recognize the significance of "total lipids" as a category as evidenced by Dietary Guidelines for Americans http://www.cnpp.usda.gov/sites/default/files/dietary_guidelines_for_americans/PolicyDoc.pdf. Typical disclosure is of total fat as a percent of calories or omega-6/omega-3 as percent of fat, percent of fatty acids or percent of calories. Further, omega-6/omega-3 are randomly present in many food sources and their preparations. Therefore, some food sources and food preparations may randomly have omega-6/omega-3 within the meets and bounds of the instant claims and some may have omega-6/ omega-3 outside the meets and bounds of instant claims. However, that random presence is not motivation for a skilled person to obtain omega-6/omega-3, as directed by instant claims, particularly because there are overwhelming opposite teachings in the art (see paragraphs [0014], [0015], [0020], and [0021] of the declaration given on September 29,

2014) and there are countless products of such teachings on the market. For these reasons, unless a reference expressly teaches the effect of minor lipid components on omega-6/omega-3 requirements and/or teaches to obtain omega-6/omega-3 as a ratio of total lipids, one cannot presume that skilled artisans will be motivated to obtain omega-6/omega-3 as a ratio of total lipids. For at least these reasons, I do not believe that references such as Mark et al, ONA, or WNA will motivate a skilled artisan to obtain omega-6/omega-3 as a percent of or ratio of total lipids.

[0014] I further declare that all statements made herein of my own knowledge are true and that statements made of information and belief are believed to be true. I further acknowledge that any willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001, and may jeopardize the validity of the application or any patent issuing therefrom.

Date: April 30, 2015

Robert B. Rucker, Ph.D.

ANNEX W:

Kent L. Erickson Testimony, May 31, 2015

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:	
Urvashi Bhagat	Examiner: Heyer, Dennis.
Application No. 12/426,034	Art Unit: 1628
Filed: April 17, 2009	Confirmation No. 3947
For: LIPID-CONTAINING COMPOSITIONS AND METHODS OF USE THEREOF	

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Kent L. Erickson, hereby declare:

[001] I received a Ph.D. in Anatomy from Oregon Health and Sciences University, Portland, OR, and I performed post-doctoral work at Oregon Regional Primate Research Center in the field of Dermatology. I served as a Scientist in the Cancer Metastasis and Treatment Laboratory at the National Cancer Research Institute, National Institutes of Health, Frederick, MD. I also served as a Researcher at the National Institute of Arthritis, Musculoskeletal and Skin Diseases of the National Institutes of Health, Bethesda, MD. I was an Underwood Fellow of the Biotechnology and Biological Sciences Council-UK and worked in the Centre for Stem Cell Biology at the University of Sheffield, UK. I served as Chair of the Department of Cell Biology & Human Anatomy at the University of California, Davis, School of Medicine for 17 years. I also served as a member of the editorial board of the Journal of Nutrition for 4 years; the American Journal of Clinical Nutrition for 6 years and the Journal of Food Science and Nutrition

for 16 years. I am currently one of the Editors of the British Journal of Nutrition as well as the Journal of Nutritional Sciences. From 1975 to 2013, I was employed as a professor by The University of California, Davis, School of Medicine; I currently hold the position of Professor and Chairman Emeritus.

[002] I am not an inventor, applicant, owner, or assignee of the above-referenced patent application. I serve on the Scientific Advisory Board (SAB) of Asha Nutrition Sciences, the assignee of the subject application. I have been allotted a modest amount of stock option grant as compensation for my SAB role. I have not received any compensation specifically for preparing this declaration. I have read the above-referenced patent application. I have also read all the other documents referenced in this declaration.

[003] I interact with many professionals in my career who possess ordinary skills in the art, such as doctors, scientists, nurses, dieticians, nutritionists, and the like ("skilled artisans"). These professionals typically have advanced degrees such as masters, Ph.Ds., and/or M.Ds. I am closely aware of the knowledge and skill levels of such professionals. I am confident in declaring that the following matters are clear to me and would be clear to other skilled artisans. I have previously given a related declaration in favor of the subject patent application on January 31, 2014.

[004] The amended independent claims 65, 91, 129 and 130 of the subject patent application are recited below.

> 65. (Currently Amended) A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids from different sources, and wherein
>
> (1) omega-6 fatty acids are 4-75% by weight of total lipids and omega-3 fatty acids are 0.1-30% by weight of total lipids; or
>
> (2) omega-6 fatty acids are not more than 40 grams.

> 91. (Currently Amended) A lipid-containing formulation, comprising a dosage of omega-6 fatty acids, wherein the omega-6 fatty acids are greater than 20% by weight of the total lipids, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of lipids from different sources, the formulation comprising polyunsaturated, monounsaturated, and saturated fatty acids, and wherein the formulation includes at least
>
> (i) one or more polyunsaturated fatty acids selected from linoleic acid (C18:2), conjugated-linoleic acid (C18:2), gamma-linolenic acid (C18:3), eicosadienoic acid (C20:2), di-homo-gamma-linolenic acid (C20:3), arachidonic acid (C20:4), alpha-linolenic acid (C18:3), stearidonic acid (C18:4), eicosapentaenoic acid (C20:5), docosapentaenoic acid (C22:5), and docosahexaenoic acid (C22:6), and

(ii) nutrients including at least
(a) one or more polyphenols, or
(b) one or more phytochemicals,
the one or more phytochemicals being selected from: phytosterols, campesterol, sitosterol, stigmasterol, organosulfur, sulfide, melatonin, lycopene, lutein, zeaxanthin, and a phenol.

129. (Currently Amended) A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of fatty acids from different sources, and wherein
omega-6 fatty acids are 4-75% by weight of total lipids and omega-3 fatty acids are 0.1-30% by weight of total lipids.

130. (Currently Amended) A lipid-containing formulation, comprising a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation to a subject, wherein at least one casing comprises an intermixture of fatty acids from different sources, and wherein
omega-6 fatty acids are not more than 40 grams and the formulation further comprises one or more polyphenols, or one or more phytochemicals selected from: phytosterols, campesterol, sitosterol, stigmasterol, organosulfur, a sulfide, melatonin, lycopene, lutein, and zeaxanthin, or vitamin E-alpha/gamma less than 0.5% by weight of total lipids, or one or more specific protein types listed in Table 21 in a dosage not more than the upper limit disclosed in the table.

[005] In light of the specification of the subject patent application, "casing" or "one or more complementing casings providing controlled delivery of the formulation to a subject" in amended claims 65, 91, 129 and 130 refer to formulations packed in casings such that controlled amounts/ dosages of the formulations are provided for consumption by the subject so that inadequate and excess intake/ingestion of the formulation is substantially avoided. This is clear from, for example, paragraphs 10, 34, 37, 60, 61, and Tables 16-19 of the specification.

[006] In light of the specification of the subject patent application, "intermixture of lipids [fatty acids] from different sources" refers to a mixture, wherein at least fatty acids and/or other lipids are integrated from at least two "different sources" to enhance the usefulness of the formulation over a "single" source. "Different sources" refers to different oils, butters, nuts, seeds, herbs, sweeteners, and/or other foods and/or their different varieties (containing different lipid profiles). This is clear from, for example, paragraphs 8, 9, 11, 21, 22-27, 30, 62 and 64 and Table 2 of the specification. For example, paragraph 30 clearly establishes that the purpose of the intermixtures is to incorporate "synergy among complementing nutrients from different sources" and "using different sources avoids concentrated delivery of specific [lipid] phytochemicals that may be harmful in excess."

[007] It is a standard practice in the art to consider a food source, such as multiple walnuts (or olives) to be a single source (i.e., single type of source). In other words, each walnut (or olive) would not be considered to be a different source of lipids from one another by skilled artisans, unless one specific variety of walnut (or olive) is added to another, different, specific variety of walnuts (or olives) to enhance usefulness of the walnut (or olive) formulation. A reference utilizing a mixture of different varieties of walnuts (olives) to enhance usefulness of the formulation would have to disclose that such a result is/was contemplated. A random mixture of single source foods, such as walnuts (or olives) would not be considered to be an "intermixture of lipids from different sources" by a skilled artisan. This simply would not be a reasonable interpretation by a skilled artisan.

[008] Lipid sources, such as oils, butters, nuts, seeds, and herbs have 100s of compounds (see http://www.ars-grin.gov/duke/ as evidence). Therefore, when lipids from different sources are intermixed, the resulting mixture will necessarily have different physical and chemical properties from a "single" source. A hypothetical mixture of lipids from Source A and lipids from Source B, where the resulting mixture has exactly the same properties as Source A or B is first practically impossible, and second, if possible, it would be an extremely complex scientific endeavor. There would be no motivation for a skilled artisan to intermix lipids from Source A and Source B to achieve exactly the same properties as Source A or Source B. Further, intermixture of exact same lipids from different sources (e.g., Walnuts and Olives) would not be a reasonable interpretation of "intermixture of lipids [fatty acids] from different sources" in light of specification by a skilled artisan. See paragraph [006] above.

[009] On January 31, 2014, in reference to US Patent No. 5,549,905 by Mark et al., I had declared that one-liter composition of Mark et al. is not the representative quantity of the total amount provided to the pediatric patient. The dosage of Mark et al. compositions to be provided to the patient has not been stated specifically but could be a few milliliters to several liters. Mark et al., do not disclose the upper or safe limit of omega-6 dosage. The declaration was written keeping in perspective that the outstanding rejections from the Office then pertained to instant Claim 65(2). In light of the currently pending rejections from the Office, I further declare as follows.

[0010] It is not possible to ascertain what Mark et al. is teaching with regard to omega-6 to omega-3 ratios. In SUMMARY OF INVENTION, column 2, lines 24-26 and 37-39, Mark et al. teach a composition having an "omega-3 to omega-6 fatty acid ratio of approximately 4:1 to 6:1" or omega-6 to omega-3 of 1:4 to 1:6. In DETAILED DESCRIPTION, column 4 lines 21-23, Mark et al. teach "The lipid profile containing such long chain triglycerides is designed to have a polyunsaturated fatty acid omega-6 (n-6) to omega-3 (n-3) ratio of approximately 4:1 to 6:1." It is not possible to ascertain omega-6 to omega-3 ratio from the table in column 4 because *only* 86% of the fatty acids are disclosed, 14% of the fatty acids are missing. Even though the table recites "TOTAL SAT/ TOTAL MONO/ TOTAL POLY" but that is clearly incorrect because the table also recites "TOTAL 86" underneath the column heading "% of Total Fatty Acids." Furthermore, based on the kind of compositions Mark et al. disclose (e.g., in column 5 and 6), it is not possible for non-fatty acid containing lipids to add up to 5.4g lipids missing from the table in column 4, because non-fatty acids containing lipids in such sources are present in extremely small amounts in 38.5g of lipids (see http://ndb.nal.usda.gov/ndb/search/list). Therefore, based on the disclosure right above the table in column 4 lines 21-23, the table in column 4 appears to disclose fatty acids of triglycerides only. Further, the ratio in column 6 line 15 of Mark et al. also appears to be based on 86% of the fatty acids in table in column 4 (C18:2 n6 12.2 ÷ C18:3 n3 = 5.08). Therefore, my expert opinion is that the omega-6 to omega-3 ratio 4:1 to 6:1 taught by Mark et al. in column 4 and N6:N3 ratio 5:1 in column 6 is in triglycerides.

[0011] Mark et al consistently discloses and claims omega-6 to omega-3 ratios in triglycerides, not in total lipids. A composition of triglycerides is the focus of entire Mark et al disclosure, for example see abstract, column 2 lines 9-11, 21-23, and 48-51, and column 4 lines 1-23, and all of the independent claims 1, 9, and 15. Mark et al. claim 6 is a dependent claim on claim 1. The claim 1 and claim 6 in combination read as follows:

> An enteral composition designed for pediatric patients comprising:
> a hydrolyzed protein source comprising approximately 12% of the total calories;
> a carbohydrate source; and
> a lipid source comprising a mixture of medium and long chain triglycerides, wherein at least 55% of the lipid source are medium chain triglycerides [. The composition of claim 1] <u>further comprising</u> an omega-6 to omega-3 fatty acid ratio of approximately 4:1 to 6:1.

Therefore, the Mark et al. omega-6 to omega-3 ratio claimed in claim 6 (and claim 17) is also in fatty acids of triglycerides.

[0012] Triglycerides are a subset of total lipids. Total lipids are well known by persons of ordinary skill in the art to include free fatty acids, mono-glycerides, di-glycerides, glycolipids, and phospholipids, which contribute fatty acids to total lipids. The lipid sources that Mark et al discloses (in column 2, 4, 5, and 6) safflower oil, canola oil, soy oil, coconut oil (MCT), residual milk fat, and soy lecithin are known to contain free fatty acids, mono-glycerides, di-glycerides, glycolipids, and phospholipids, which contain omega-6 and omega-3 fatty acids (*Chen et al., Critical Reviews in Food Science and Nutrition, 51:901–916 (2011); Chaiyasit et al., Critical Reviews in Food Science and Nutrition, 47:299–317 (2007)*). Soy lecithin, for example, can contain ~90% glycolipids and phospholipids, and the soy lecithin phospholipids can be rich in omega-6 and omega-3 fatty acids (*Scholfield CR, Journal of the American Oil Chemists' Society, vol. 58, no. 10 (October 1981), p. 889-892; ALC, American Lecithin Company, Downloaded from Internet on December 28, 2014*). Thus, Mark et al entire disclosure discloses omega-6 to omega-3 fatty acid ratios in triglycerides only, and fails to count fatty acids from free fatty acids, mono-glycerides, di-glycerides, glycolipids, and phospholipids in its compositions and omega-6 to omega-3 ratios. When omega-6 to omega-3 ratio is 4:1 to 6:1 in triglycerides, it can be 1:4 to 1:6 in total lipids, as recited in column 2 lines 24-26 and 37-38 of Mark et al. Thus, in my expert opinion, Mark et al has not disclosed omega-6 to omega-3 ratio of 4:1 or greater in total lipids as in instant claims 65, 129, and 130.

[0013] Further, column 4, lines 40-60 of Mark et al. disclose 12.2% C18:2 n6, which is linoleic acid (LA), and 2.4% C18:3 n3, which is alpha-linolenic acid (ALA), which is <u>not</u> the disclosure of 12.2% omega-6 fatty acids and 2.4% omega-3 fatty acids. Likewise, the amount of linoleic acid 4.7g, and alpha-linolenic acid 0.9g is disclosed, not that of total omega-6 and total omega-3 fatty acids. The percentage or amount (dosage) of total omega-6 or omega-3 cannot be calculated because the table in column 4 *only* discloses 86% of the fatty acids; 14% of fatty acids are missing from the table.

[0014] Furthermore, Mark et al. define "lipids" as "safflower oil, canola oil, soy oil, coconut oil, residual milk fat, and soy lecithin" (see column 5 last paragraph), however, these recited substances are not 100% lipids as per conventional definition of lipids (*Fahy et al. J. Lipid Res. 2005. 46:839–861; The Nomenclature of Lipids, J Lipid Res. 1978 Jan;19(1):114-28*). The "lipid" recited by Mark et al. are known to contain non-lipids (see *Chen and Chaiyasit Supra*), even if in small amounts. It is evident from Mark et al. column 5 and 6 that Mark et al, simply add weight of sources of lipids (CANOLA OIL 13%, SOY OIL 16%, COCONUT OIL MCT 60%, RESIDUAL MILK FAT 6%, SOY LECITHIN 5%) to arrive at 38.5g/L "lipids". My assessment is that small part of missing 5.4g of "lipids" in table in column 4 may not be lipids as conventionally defined, but majority of the 5.4g missing lipids are fatty acids which contain omega-6 and omega-3 fatty acids. Additionally, Mark et al. has a separate category where lipid vitamins are listed in column 6. Therefore, Mark et al "total lipids" cannot be compared to "total lipids" in instant claims, which refer to conventional definition of lipids.

[0015] Furthermore, I do not believe that the amounts of LA and ALA disclosed in table in column 4 of Mark et al. are "dosages" because there is no disclosure anywhere in Mark et al. regarding what might be suitable daily dosages of omega-6 or omega-3 for children between the ages of 1-10 years. It should be noted that one-year-old child can have a body weight that is 100 lbs. less than a 10-year old child, with dramatically different omega-6 and omega-3 daily dosage requirements. In column 5 Mark et al. state "the composition of the present invention meets NAS-NRC RDAs for children ages 1-10 years in 1000 calories. The high vitamin and mineral concentration of the present invention is of practical benefit because typical feeding regimens (e.g. 50mL/hour for 20 hours/day) will meet all needs. …none of the vitamin or mineral concentrations are so high that there is any risk of approaching toxic levels, even at 2000-2500 kcal per day." As evident, the statement "typical feeding regimens (e.g. 50mL/hour for 20 hours/day) will meet all needs" is in context of vitamin and mineral concentration, not omega-6 and omega-3 dosage. Also caloric requirement for a 1-10-year old child varies from 800-2600 per day. Therefore, feeding regimen of Mark et al. compositions may be few milliliters for a 1-year old child and few liters for a 10-year old child. In fact, Mark et al. state feeding regimen may be 2 or 2.5 liters per day (2000-2500 kcal per day) without specifying any age group or upper limit in liters. Therefore, as declared previously (see paragraph [009] above) dosage of

Mark et al. compositions to be provided to the patient has not been stated specifically but could be a few milliliters to several liters. Therefore, Mark et al., simply disclose a concentration of LA and ALA in the composition, but not the upper or safe limit of omega-6 dosage. In contrast instant specification consistently teaches daily dosages with specific directions on how to practice the daily dosages throughout the disclosure. In light of the specification, the reference to "dosage" in instant claims is to achieving correct daily dosage via supplements and/or full diet (for example, see paragraphs 34-38).

[0016] Mark et al is not a credible reference. The reference uses terms such as "Total" and "lipids" negligently as in the table in column 4 and in column 5 last paragraph, and the reference fails to teach compositions with total omega-6 and omega-3 in total lipids, even though minor omega-6 and omega-3 constituents of free fatty acids, mono-glycerides, di-glycerides, glycolipids, and phospholipids can have major impact on the properties of the formulation and health of subject consuming such formulations. A practitioner using Mark et al. will not know what omega-6 to omega-3 ratios to use in total lipids and how much omega-6 and omega-3 to put into Mark et al formulations, and how to practice omega-6 and omega-3 dosages because of negligent use of terms, and gaps and inconsistencies in the disclosure.

[0017] Therefore, due to the preponderance of evidence in paragraphs [009]-[0015] above, in my expert opinion Mark et al. is not an operable reference.

[0018] "Olives" is one of the ~130 foods listed on the site www.whfoods.com. The archived version of "Olives" (published March 14, 2006) is http://web.archive.org/web/20060314112112/http://www.whfoods.com/genpage.php?pfriendly=1&tname=foodspice&dbid=46. Olives In-depth Nutrient Analysis "ONA" (published March 14, 2006) is the associated page http://web.archive.org/web/20060314112106/http://www.whfoods.com/genpage.php?tname=nutrientprofile&dbid=111 disclosing nutrients in Olives. There is no suggestion in either Olives or ONA for "intermixture of lipids [fatty acids] from different sources," as recited in instant claims in paragraph [004]. As a skilled artisan, I consider one or more servings of olives to be a single source and I do not consider each olive to be a different source of lipids [fatty acids] from one another. Unless there is a specific, different type of olive added to the olives to enhance usefulness of the olives (as discussed above). There is no such suggestion of such a combination in either Olives or ONA.

[0019] "Walnuts" is one of the ~130 foods listed on the site www.whfoods.com. The archived version of "Walnuts" (published November 9, 2006) is http://web.archive.org/web/20061109221131/http://www.whfoods.com/genpage.php?pfriendly=1&tname=foodspice&dbid=99. Walnuts In-depth Nutrient Analysis "WNA" (published November 9, 2006) is associated page http://web.archive.org/web/20061109221127/http://www.whfoods.com/genpage.php?tname=nutrientprofile&dbid=132 disclosing nutrients in Walnuts. There is no suggestion in either Walnuts or WNA for "intermixture of lipids [fatty acids] from different sources" as recited in the instant claims and in paragraph [004]. As a skilled artisan, I consider one or more servings of walnuts to be a single source and I do not consider each walnut to be a different source of lipids from one another. Unless there is a specific, different type of walnut added to the walnuts to enhance usefulness of the walnuts (as discussed above). There is no such suggestion of such a combination in either Walnuts or WNA.

[0020] It is important to note that the significance of "total lipids" as a category is not well understood in the art, even though the definition/classification of lipids is very well known (see *The Nomenclature of Lipids, J Lipid Res. 1978 Jan;19(1):114-28*). The effect of important lipid components, such as various phytochemicals in health and physical and chemical properties of formulations is not well understood. Food labeling practices routinely ignore important lipid components, as evidenced by Mark et al, ONA, WNA, and whfoods.com in general. Further, various authoritative nutrient databases (such as USDA databases) similarly disperse lipids over various categories and miss to report several important lipids and significance of "total lipids" as a category. Even authoritative guidelines do not recognize the significance of "total lipids" as a category as evidenced by FDA Nutrition Facts Labeling requirements (http://www.fda.gov/Food/ IngredientsPackagingLabeling/ LabelingNutrition/ucm274593. htm#see3) and Dietary Guidelines for Americans http://www.cnpp.usda.gov/sites/default/files/dietary_guidelines_ for_ americans/ PolicyDoc.pdf. Typical disclosure is of total fat and omega-6/omega-3 as percent of fat, percent of fatty acids or percent of calories. For these reasons, unless a reference expressly teaches the effect of various lipid components on omega-6/omega-3 requirements and/or specifically teaches to obtain omega-6/omega-3 as a ratio of total lipids, one cannot presume that

skilled artisans will be motivated to obtain omega-6/omega-3 as a ratio of total lipids. For at least these reasons, I do not believe that references such as Mark et al, ONA, or WNA will motivate a skilled artisan to obtain omega-6/omega-3 as a percent of or ratio of total lipids.

[0021] Further, omega-6/omega-3 are randomly present in many food sources and their preparations. Therefore, some food sources and food preparations may randomly and inconsistently have omega-6/omega-3 within the meets and bounds of the instant claims and some may have omega-6/ omega-3 outside the meets and bounds of instant claims. However, that random and inconsistent presence is not motivation for a skilled person to obtain omega-6/omega-3, as directed by instant claims, particularly because there are overwhelming opposite teachings in the art (*Lands, Nutrition Reviews 1986:44-6:189-95; Lands, Ann. N.Y. Acad. Sci. 1055: 179–192 (2005); Simopoulos, Ann Nutr Metab 1999;43:127–130; Hamazaki et al. World Rev Nutr Diet. Basel, Karger, 2003:92:109–132*) and there are countless products of such teachings on the market. Therefore, random presence of omega-6 and omega-3 cannot be considered to be the "a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater, contained in one or more complementing casings providing controlled delivery of the formulation to a subject…", wherein dosages are controlled and wherein ratio of omega-6 and omega-3 fatty acids to total lipids is controlled.

[0022] I further declare that all statements made herein of my own knowledge are true and that statements made of information and belief are believed to be true. I further acknowledge that any willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001, and may jeopardize the validity of the application or any patent issuing therefrom.

Kent L. Erickson Date: May 31, 2015

Kent L. Erickson, Ph.D.

ANNEX X:

Kent L. Erickson Testimony, July 14, 2015

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:	
Urvashi Bhagat	Examiner: Heyer, Dennis.
Application No. 12/426,034	Art Unit: 1628
Filed: April 17, 2009	Confirmation No. 3947
For: LIPID-CONTAINING COMPOSITIONS AND METHODS OF USE THEREOF	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPLICANT'S SUMMARY OF INTERVIEW

Sir:

This communication provides summary of the Interview held on July 14, 2015 at 2pm Eastern time.

cc. Examiner, Dennis Heyer
Supervisory Examiner, Wu Cheng (Winston) Shen
Director TC 1600, Daniel Sullivan

INTERVIEW SUMMARY

Interview participants:

On behalf of USPTO: **Daniel Sullivan, Dennis Heyer, Winston (Wu-Cheng) Shen**

On behalf of Applicant: **Urvashi Bhagat, Inventor**

Kent Erickson, Scientific Advisor to Applicant

Robert Rucker, Unaffiliated Skilled Person

1. Applicant asserted that claim interpretation must be in light of specification, and as per arguments and evidence of record. The Applicant has specified several times in responses to Office actions how the Applicant's claims are to be interpreted and submitted evidence as to how a skilled person would interpret the claims (declarations from Drs. Das, Rucker, and Erickson). For example, in light of specification and arguments and evidence of record, "different sources" means different oils, butters, nuts, seeds, herbs, sweeteners, and/or other foods and/or their different varieties (containing different lipid profiles), and that a food source, such as multiple "walnuts" or "olives" is "single" source unless specific varieties (of walnuts/olives) containing different lipid profiles are mixed. The entire specification is full of evidence supporting this interpretation. Applicant also reviewed the parts of the specification in which this is evident (for example, para 9, 22, and 30). **It is on record how the claims are to be interpreted, then that's how the claims are to be interpreted.**

   Examiner Heyer said that the feature "intermixture of lipids from different sources" is broader than the previously examined feature "intermixture of fatty acids from different sources" in claim 135 and 138. Applicant notes that the amended claims 65 and 91 are still narrower than as previously examined. Further, the feature "intermixture of lipids from different sources" is inherent in previously examined claims 61 and 128.

2. Applicant asserted that USC 101 issues with respect to claims 65, 91, 129, and 130, are overcome at least due to the following:

   2.1. Claims are not "directed to" natural phenomenon. "Intermixture of lipids [fatty acids] from different sources" do not occur in nature and are not judicial exceptions.

   2.2. Chemical, physical, structural, and other properties of "intermixture of lipids [fatty acids] from different sources" are markedly different from their naturally occurring counterparts.

      2.2.1. For example, oils that occur inside natural products (e.g., olives or walnuts) have different chemical and physical properties than extracted oils, and intermixed lipids from olives and walnuts have different properties from olives and walnuts. In an intermixture exposure to oxygen is different than inside walnuts or olives, which affects FFA and Tgl composition. Also in intermixtures lipids self-assemble into colloids/ structures affecting properties. See Chen and Chaiyasit and declarations submitted. Minor lipid changes have major effect. There are numerous implied, unexpected and unobvious differences. A small change can result in markedly different characteristics from nature (December 2014 Guidance issued by USPTO OPLA pp. 74623, col 3 para 1).

2.2.2. In a composition of matter involving multiple molecules, the qualifying criterion is not whether or not there is structural change in any given molecule in comparison to its naturally occurring counterpart, but the structure of overall composition.

2.2.3. The only way to obtain these intermixtures is either to extracts lipids from different sources and then mix them or to mix the animal/plant tissue/organs themselves. Either way there are structural differences as compared to natural products. MPEP 2113 states that the structure "implied" by process is relevant, and "unobvious difference" and "unexpected properties" are the dispositive issue and the term "intermixture" is capable of construction as a structural limitation.

2.2.4. Mixing Source A and Source B to achieve the same properties as Source A or B is first practically impossible and second would not enhance the usefulness of the formulation over Source A or B, and does not fit the claim interpretation as specified by the Applicant. **Further, there would be no motivation for a skilled person to mix Source A and B only to end up with source A or B, or a mixture that is substantially the same as Source A or B**.

2.3. Functions (biological and pharmacological) of products of instant claims are different from products of nature. Nature is extremely variable and unpredictable in nutrient content. Nature does not formulate lipids from different sources to enhance usefulness, provide dosages and controlled delivery to a subject. This is discussed at length in the response filed on May 1, 2015 (pages 59-61). A small change can result in markedly different characteristics from nature (Guidance pp. 74623, col 3, para 1).

2.4. Combination of the elements, "formulation", "dosage", "controlled delivery to a subject", "casings", and "intermixture of lipids [fatty acids] from different sources", amount to significantly more than any judicial exception. (Guidance pp. 74624, col 1 last para and col 2 para 1)

2.5. Claims are directed to not well-understood, non-routine, and non-conventional features, which confers eligibility based on case-law:

2.5.1. omega-6 to omega-3 ratio of 4:1 or greater

2.5.2. omega-6 and omega-3 formulations by weight of total lipids

2.5.3. omega-6 fatty acids dosage not more than 40 grams

2.5.4. omega-6 fatty acids are greater than 20% by weight of the total lipids

2.6. Claims are inventive and lead to improvements in the technical field, which confers eligibility based on case-law:

2.6.1. Overwhelming opposite teaching in the art versus instant claims

2.6.2. Mass confusion and erroneous teachings in the art

2.6.3. Poor expectation of success using teachings of the prior art

2.6.4. Unexpected results disclosed in the current patent application

2.6.5. Claims are directed to solving a long-felt, critical, unmet need

2.6.6. The claimed inventions have the potential of making very significant advancement in the art and enhancing public health

2.7. Claims are similar to eligible Nature Based Product Examples issued by USPTO OPLA, December 2014. See Example 1: Gunpowder and Fireworks: Product Claims That Are

Not Directed To An Exception, and so confirmed by OPLA. See full discussion on pages 69-70 of the response filed on may 1, 2015.

Mr. Sullivan said that the "intermixture of lipids from different sources" could be substantially the same as source A or B. However, Applicant has submitted arguments and evidence that there would be no motivation for a skilled person to mix Source A and B to end with a mixture that is substantially the same as Source A or B.

Applicant further asserted that the claims are eligible based solely on any one of the criteria above. It is not necessary for the claims to meet every single criteria listed above. However, all of the above criteria are met by claims 65, 91, 129 and 130

3. USC 102 Issues

3.1. Applicant asserted that USC 102 issues with respect to "Olives" and "Walnuts" and instant claims 65, 91, 129, and 130, are overcome at least due to the following:

3.1.1. The feature, "an intermixture of lipids [fatty acids] from different sources" is not present in "Olives" or "Walnuts", as interpreted in Applicant's claims. It is evident from the specification, put on record by the Applicant, and testified by skilled persons that each walnut (or olive) would not be considered to be a "different source" of lipids from one another by skilled artisans, unless one specific variety of walnut (or olive) is added to another, different, specific variety of walnuts (or olives) to enhance usefulness of the walnut (or olive) formulation.

3.1.2. There is no suggestion of different sources (different varieties of olives or walnuts) to enhance usefulness of the formulation over a single source in "Olives" or "Walnuts". Inherency cannot be based on possibilities.

3.1.3. MPEP 2113 states that the structure "implied" by process is relevant, and "unobvious difference" and "unexpected properties" are the dispositive issue and the term "intermixture" is capable of construction as a structural limitation.

3.1.4. Whfoods.com, i.e. the webpages which disclose "Olives" and "ONA", and "Walnuts" and "WNA" teach mixtures of foods (including lipids from different sources), wherein overall ratio of omega-6 to omega-3 is around 2:1.

3.1.5. Neither "olives" nor "walnuts" disclose part-to-part relationships set forth in the instant claims that give the claims their meaning and life. At least the following elements are not **expressly/unequivocally** present in the reference let alone not arranged or combined the same way as defined in instant claims:

- an intermixture of lipids [fatty acids] from different sources
- a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater [in total lipids]
- omega-6 fatty acids are 4-75% by weight of total lipids and omega-3 fatty acids are 0.1-30% by weight of total lipids
- omega-6 fatty acids are not more than 40 grams
- omega-6 fatty acids are greater than 20% by weight of the total lipids

3.1.6. The concept of "inherent disclosure" does not alter the requirement that all elements must be disclosed in an anticipatory reference in the same way as they are arranged or combined in the claim. " *Transclean Corp. v. Bridgewood Servs., Inc.*, 290 F.3d 1364, 1373 (Fed. Cir. 2002).

3.1.7. The requirement that the prior art elements themselves be "arranged as in the claim" means that claims cannot be "treated . . . as mere catalogs of separate parts, in disregard of the part-to-part relationships set forth in the claims and that give the claims their meaning." *Lindemann Maschinenfabrik GMBH v. Am. Hoist & Derrick Co.*, 730 F.2d 1452, 1459 (Fed. Cir. 1984)

3.2. Mark et al. with respect to instant claims 82 and 130
Applicant asserted that instant claims 82 and 130 include features that are not even mentioned in Mark et al. Therefore, the claims are allowable without further analysis. Examiner Heyer said that the Office agrees with that assertion.

3.3. Applicant asserted that instant claims 65 and 129 are allowable with respect to Mark et al. at least due to the following:

3.3.1. The entire disclosure of Mark et al. is focused on composition of triglycerides. Column 4 specifies omega-6 to omega-3 ratio of 4:1 to 6:1 in triglycerides.
3.3.2. **The table in column 4 either discloses fatty acids of triglycerides only or the data in the table is corrupted and the table is inoperable**. No teaching regarding omega-6 to omega-3 ratios, concentrations or amounts in total lipids can be obtained from the table because of the missing fatty acids. This has been testified in declarations from Drs. Rustagi, Rucker, Das, and Erickson.
3.3.3. The omega-6 to omega-3 ratios in column 2 versus column 4 are inconsistent.
3.3.4. Claim 6 and 17 must be read together with independent claims 1 and 15 upon which they depend, and interpreted in light of Mark et al specification in column 2 and column 4. Thus, claim 6 and 17 also disclose omega-6 and omega-3 in triglycerides.
3.3.5. Dosage is known to be distinct from concentration was confirmed by Dr. Erickson (also see http://www.iupac.org/publications/ci/2001/march/risk_assessment.html#author). There is no reference to dosage in Mark et al. Dosage of n6/n3 can be significantly different for a 1-year old vs. a 10-year old. There is no teaching (enablement) regarding this in Mark et al. The “typical feeding regimen” is in reference to tolerance of vitamins and mineral concentration, not n6 and n3 dosages.
3.3.6. Mark et al define “lipids” differently than convention (col 5 last para and col 6), hence Mark et al “total lipids” are different from instant claims.
3.3.7. “Express/unequivocal” teaching as in instant claims is not available from any one of the examples, situations, claims, or parts, or even in combination of the entire disclosure of Mark et al. Claims cannot be "treated . . . as mere catalogs of separate parts, in disregard of the part-to-part relationships set forth in the claims and that give the claims their meaning." *Lindemann Maschinenfabrik GMBH v. Am. Hoist & Derrick Co.*, 730 F.2d 1452, 1459 (Fed. Cir. 1984). At least the following elements are not **expressly/unequivocally** present in the reference let alone not arranged or combined the same way as defined in instant claims:
    - a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater [in total lipids]
    - omega-6 fatty acids are 4-75% by weight of total lipids and omega-3 fatty acids are 0.1-30% by weight of total lipids
    - omega-6 fatty acids are not more than 40 grams

3.3.8. "Unless all of the same elements are found in exactly the same situation and united in the same way to perform the identical function in a single prior art reference, there is no anticipation**."** In General Battery Corp. v. Gould, Inc., 545 F. Supp. 731, 740 (D. Del. 1982)

3.3.9. "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." In re Fine, 837 F.2d 1071, 1075 (Fed. Cir. 1988).

3.3.10. Dr. Erickson testified on the call (in addition to his testimony on record) that Mark et al. is not a credible reference. He said that if the reference was sent to him for review he would not have approved it for publication due to many discrepancies and deficiencies, specifically due to the opposite omega-6 to omega-3 ratio teaching in column 2 versus column 4 and missing fatty acids in the table in column 4.

3.4. Examiner Heyer said that we are all in agreement that fatty acids are missing from the table in column 4 of Mark et al. but that Office does not have a lab to obtain lab results of the formulations. However, Applicant asserted that more than sufficient evidence including testimony from **four** skilled persons has been submitted that Mark et al do not anticipate instant claims. (It is noted that Mark patent is expired, the related product may not be on the market. Further, lab results will not provide sufficiently specific teaching to constitute anticipation, irrespective of other findings of the lab results.)

Applicant pointed out that Mark et al. omega-6 to omega-3 ratio in column 6 is also based on 86% of the fatty acids from the table in column 4, because it precisely tallies. Examiner Heyer said that he would look at the possibility if additional omega-6 and omega-3 missing from the table in column 4 would shift the ratio in the Lipid Profile of Mark et al. outside the scope of Claim 65. **However, that is impossible to determine because the reference does not disclose lipid profile of sources used and there is extreme variability of lipids in lipid sources (see evidence of record including Dr. Erickson's declaration, Jan 2014). Inherency cannot be based on possibilities, missing descriptive matter has to be present. Further, for USC 102 rejection the prior art reference has to disclose every single limitation of the claimed invention exactly as in the claims, with the same part-to-part relationships as in the claims, which give claims life and meaning based on well-established case law**. In case of instant Claim 65 and 129, there is a dosage of omega-6 to omega-3 at a ratio of omega-6 to omega-3 (not linoleic acid, LA, to alpha-linolenic acid, ALA) of 4:1 or greater, wherein omega-6 fatty acids (not LA) are 4-75% by weight of total lipids and omega-3 fatty acids (not ALA) are 0.1-30% by weight of total lipids or omega-6 fatty acids (not LA) are not more than 40 grams. The specific part-to-part relationships, i.e., the essence of the instant invention that give life and meaning to the claims are not disclosed by Mark et al. Also see preponderance of evidence above in points 3.3.1-3.3.10 and on record.

Examiner Heyer said that then there may be a question of obviousness with respect to Mark et al. However, obviousness rejection would be improper in this case, because of overwhelming opposite teaching in the art and from Mark et al itself (column 2).

4. Applicant asserted that Applicant has disclosed a very important invention. The limitations in claims 65, 91, 129, and 130 are meaningful limitations, claim scope is commensurate with size of the problem to be solved, and the claims are allowable due to arguments and evidence presented above and on record.

   Following discussion is not verbatim from the interview, but was discussed in essence during the interview and is on record:

   Mr. Sullivan stated that Office has a duty to protect the public, therefore patent grant has to be carefully considered. Applicant appreciates this. However, considering that the problem to be solved is an ~80-year old critical problem, that the prior art (including industry and government) has failed to solve the problem (see evidence of record), and that due to the complexity involved public by and large cannot solve this problem, Applicant has the right and should be given patent protection to solve the problem, which requires investment of significant capital and other resources on part of the Applicant. It is reasonable for the Applicant to request sufficient protection for the term of the patent in order to make this a viable business and effectively implement the solutions. **Denying Applicant its legal rights is improper and it does not protect the public. It subjects the public to business as usual, i.e. mass confusion and erroneous teachings in the art.**

   Applicant has previously submitted on record that narrow nutrition patents are not in the best interest of the public, they lead to touting of nutrients/sources out-of-context. Applicant believes that narrow nutrition patents have previously caused great harm to the public. **If momentous changes are not made, it will get all the more complicated to turn the situation around**. Nutrition is complex, but not as complex as the labyrinth of cure, the latter can be curtailed via foresight in patent policy.

   Further, Office has a duty to protect the Applicant's intellectual property. Applicant has suffered due to the prolonged prosecution, which has cost the Applicant reduced patent term and resources, and it has delayed the solutions from reaching the public. Office is forcing the Applicant to file multiple Divisional Applications, which will escalate the problem. The disclosed solutions are interrelated. If they cannot be made available contemporaneously, it will limit or even jeopardize public benefit.

   Mr. Sullivan suggested that the Applicant file an appeal. He said, "we would like this case to go to appeal because we want to see how the Board decides this case." Applicant finds that to be improper because the Office is aware that the legal requirements are met. It is inappropriate to send a case to appeal to "see how the Board decides" because it inappropriately further prolongs prosecution. Further, it is inappropriate to hold scope of the invention against the Applicant. If a significant problem is solved by an Applicant that is reason to advance the case faster not to slow it down. Holding such inventions back is tragic because it defeats the very purpose of patents, which is to solve major problems.

In summary, claims 65, 91, 129, and 130 meet statutory requirements and should be promptly granted.

Kent L Erickson

Verified, Kent L. Erickson

CONCLUSION

This communication is filed to fulfill Applicant's duty to record substance of the interview. Should any issues remain that the Examiner believes may be dealt with in a telephone conference, he is invited to contact the Applicant at 650-322-7861 or 650-906-7811.

Dated this 21st day of July, 2015.

Respectfully submitted,

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ANNEX Y:

Bhagat U. Das UN., Arch Med Sci 2015; 11, 4: 807–818

Potential role of dietary lipids in the prophylaxis of some clinical conditions

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Abstract

An imbalance of dietary lipids may potentially have a significant role in the pathobiology of some chronic diseases. Public health dietary fat recommendations have emphasized that low saturated fat, high monounsaturated fat, and high polyunsaturated fat with a lower ω-6 to ω-3 fatty acid ratio intake are necessary for normal health. However, such universal recommendations are likely to be hazardous, since the outcome of recommended lipid intake may depend on the consumption of other important dietary constituents that have an important role in the metabolism of lipids. In addition, consumption of fatty acids as per the individually tailored specific requirements in the context of other nutritional factors may have the potential to stabilize hormones, mood and sleep, and minimize adverse events. In support of this proposal, we review various factors that influence fatty acid metabolism, which need to be taken into consideration for appropriate utilization and consequently prevention of various diseases.

Key words: prevention, fatty acids, antioxidants, phytochemicals, inflammation, cytokines, unsaturated fatty acids, prostaglandins.

Introduction

Both qualitative and quantitative imbalances in the intake and metabolism of dietary fats have been implicated in a number of chronic diseases including cardiovascular diseases (CVD), obesity, diabetes mellitus (DM), and rheumatoid arthritis (RA) [1–5]. Thus far, in order to overcome these imbalances, the suggested preventative solutions have focused on the delivery of one or more lipids in the form of supplementation of ω-3 fatty acids [2], conjugated-linoleic acid (LA) [6], and γ-linolenic acid [7]; and other recommendations include enhanced use of certain oils, such as olive oil and canola oil, in order to deliver greater amounts of monounsaturated fatty acids and α-linolenic acid [1, 2]. Reduction in saturated fatty acid consumption has also been recommended [1, 3, 4]. Though these broad health recommendations appear to have reduced the risk of some diseases, they are not uniformly beneficial and in fact, may actually enhance the risk of some disease. For instance, it was reported that replacing dietary saturated fat with ω-6 linoleic acid, for the secondary prevention of coronary heart disease and death, showed no evidence of cardiovascular benefit [8]. This may be interpreted to mean that other dietary components that are essential for its (LA) beneficial action also need to be obtained to derive the beneficial action of increased

consumption of LA. It is noteworthy that LA is oxidized to form oxidized LA metabolites (OXLAMs) that are the most abundant oxidized fatty acids in oxidized low density lipoprotein, which are potentially more atherogenic than unmodified low density lipoprotein. This implies that various factors that have a modulatory influence on LA metabolism such as antioxidants [9–12], phytochemicals [13–18], minerals [19], gender [20, 21], age [22], and genetics [23] play a significant role in bringing about its (LA) beneficial action. Thus, there are many variables that modulate the metabolism of various fatty acids. Furthermore, it will be difficult for consumers to calibrate on a daily basis the demands of the body for various fatty acids. This is so since the requirements of various biologically active unsaturated fatty acids change depending on age, gender, and various life style factors. It is possible that there could exist differences in the requirements of various fatty acids and their co-factors even among members of the same family. In view of this, it is important to evolve precise personalized yet broad based dietary lipid program(s) that are easy to implement to prevent various diseases. It is the purpose of this review to discuss various factors that influence fatty acid metabolism based on which guidelines to develop customized lipid programs can be drawn and recommended.

Metabolism of essential fatty acids

Dietary lipids include fatty acids, sterols, carotenoids, and vitamins A and E. A good review of the terminology, sources, digestion, metabolism, and physiological actions of lipids is provided by Ratnayake and Galli [24]. In summary, linoleic acid (LA, C18:2) and α-linolenic acid (ALA, C18:3) are essential fatty acids (EFA) since humans cannot synthesize them *de novo* but they are essential for survival. Though both LA and ALA are biologically active [1, 24], they need to be converted to their long-chain metabolites to gain benefit of their full potential [25, 26]. Linoleic acid, the ω-6 EFA, is elongated and desaturated to give rise to its long-chain metabolites: γ-linolenic acid (GLA, C18:3), dihomo-gamma-linolenic acid (DGLA, C20:3), and arachidonic acid (AA, C20:4). Dihomo-gamma-linolenic acid forms the precursor of 1 series prostaglandins (PGs), whereas AA is the precursor of 2 series PGs, thromboxanes (TXs), and 4 series leukotrienes (LTs). On the other hand, ALA is the precursor of its long-chain metabolites eicosapentaenoic acid (EPA, C20:5) and docosahexaenoic acid (DHA, C22:6) of the n-3 family. Eicosapentaenoic acid gives rise to 3 series PGs and TXs, and 5 series LTs. LA, GLA, DGLA, AA, ALA, EPA, and DHA are all polyunsaturated fatty acids (PUFA), while only LA and ALA are EFAs. All EFAs are also PUFAs but all PUFAs are not EFAs. Eicosanoids (PGs, TXs and LTs) have many actions and are involved in several physiological and pathological processes, some of which include: blood vessel constriction, dilation, blood pressure regulation, platelet aggregation, and modulation of inflammation, etc. [24, 27]. In general, eicosanoids derived from AA have more potent actions compared to those derived from EPA, though there are exceptions to this generalization [28]. Additionally, AA, EPA, and DHA are precursors to lipoxins, resolvins, and neuroprotectins that have potent anti-inflammatory actions [24]. Polyunsaturated fatty acids and their products including eicosanoids, lipoxins, resolvins and protectins modulate a number of biological functions by their ability to form an active component of cell membranes and by influencing pinocytosis, ion channel regulation and gene expression [24, 27].

α-Linolenic acid, LA, and oleic acid (OA) undergo oxidative desaturation by the same set of enzymes – delta-6-desaturase (Δ^6) and delta-5-desaturase (Δ^5) – to give rise to their respective – PUFAs [29, 30]. Among the three fatty acids, ALA is preferentially desaturated, LA second, and OA third (ALA > LA > OA) [29, 31]. This affinity of the Δ^6 and Δ^5 to their substrate has important therapeutic implications since changes in the availability and/or increases or decreases in one substrate can have a profound effect on the metabolism of the other substrates. In view of this, consumption of the right balance of dietary fatty acids is important and this constituted a vigorous debate as to what is the right proportion or ratio of *n*-3, *n*-6 and *n*-9 to be consumed for their optimal utilization and usefulness in the body. A number of studies have discussed the importance of maintaining a balance between ω-6 and ω-3 fatty acids in human nutrition for optimal function of various tissues specifically taking into consideration the eicosanoids produced from ω-6 and ω-3 fatty acids due to their significant divergent actions especially in inflammation, among other reasons [32–34]. The present pattern of consumption indicates that the ratio between ω-6-to-ω-3 ratios is ~15–17 : 1 in Western diets, which has been cited as one of the important dietary factors that has led to the increase in the incidence of modern chronic diseases such as insulin resistance, atherosclerosis, type 2 diabetes mellitus and cancer [2, 33].

For example, studies have shown that adult human brain consumes AA and DHA at rates of 17.8 and 4.6 mg/day, respectively (ratio – 3.87 : 1), respectively [35]. Further, it was shown that most adult human tissue contains approximately 10 times AA as compared to DHA [36]. This demonstrates that AA requirement is 4 to 10 times that of DHA. Furthermore, it has been shown to be

equally competitive, LA and ALA should be in the ratio of 14 : 1 [32]. Based on this logic the ratio between ω-6-to-ω-3 of 15–17 : 1 in diets is not the problem, the problem is the other factors that influence the metabolism of ω-6 and ω-3.

A substantial number of studies revealed additional complexity in the metabolism of essential fatty acids and their long-chain metabolites besides the complexity that exists as a result of changes in the ratios among fatty acids. For instance, previously we noted that when Sprague-Dawley rats (200–220 g) were fed a fat-free semi-synthetic diet supplemented with 10% (by weight) of different combinations of evening primrose oil (EPO), a rich source of LA and γ-linolenic acid, and polepa (POL), a marine oil rich in eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids (the combinations of supplement were 9% EPO-1% POL, 8% EPO-2% POL, 7% EPO-3% POL, 6% EPO-4% POL and 5% EPO-5% POL) it was observed that animals fed higher proportions of POL consistently contained higher levels of DGLA ($p < 0.05$) and lower levels of AA ($p < 0.05$). Thus, an inverse relationship between AA/DGLA ratio and EPA levels was found to exist ($r = –0.765$ in plasma and –0.792 in liver [37]. In a similar fashion, an interaction may occur between ALA/EPA ratio and AA levels. Such an interaction among various *n*-3 and *n*-6 fatty acids makes it difficult to anticipate how the metabolism of PUFAs and formation of various eicosanoids occur and at times difficult to foresee and predict the products that are likely to be formed from various PUFAs under different physiological and pathological conditions. Despite this complex interaction among various *n*-3 and *n*-6 fatty acids, certain generalizations are possible, though arriving at some of these conclusions needs to be done rather cautiously. This implies that in all clinical conditions multiple changes in the concentrations of plasma and/or tissue fatty acid profile may occur and no single fatty acid could serve as a marker of any particular disease. For instance, it was reported that high proportions of palmitic acid (16:0), palmitoleic acid (16:1), and DGLA, and a low proportion of LA, AA, EPA and DHA, occur in the plasma/serum in type-2 diabetes [3, 34, 38, 39], myocardial infarction [40, 41], stroke [42], left ventricular hypertrophy [43], and metabolic syndrome [44, 45]. Increased activity of SCD (stearoyl CoA desaturase, also known as delta-9-desaturase, which desaturates saturated fatty acids (SFA) to form monounsaturated fatty acids (MUFA)), and low Δ^5 activity have also been described to be independently associated with increased risk for cardiovascular diseases, insulin resistance and low-grade systemic inflammation, and cardiovascular and total mortality [46, 47]. Warensjo *et al.* observed an independent association between desaturase activity indices and mortality risk. They suggested that altered endogenous desaturation might contribute to the risks [47]. Others have suggested that a defect in Δ^6 and Δ^5 may be a factor in the initiation and progression of insulin resistance and atherosclerosis and their associated diseases such as obesity, diabetes mellitus, and hypertension [3, 40, 48, 49]. The complexity of the involvement of PUFAs in various diseases is further evident from the studies with regard to the role of linoleic acid (LA, 18:2 *n*-6) and its metabolites specifically in cardiovascular diseases. For instance, studies performed both in experimental animals and humans in the early 1950s and 1960s showed that increased intake of saturated fats increases plasma cholesterol levels and leads to the development of hypercholesterolemia, while enhanced intake of unsaturated fatty acids including LA reduces plasma and tissue cholesterol levels [50–56].

Factors influencing the metabolism of essential fatty acids

It is well documented that various dietary and non-dietary factors modulate the metabolism of EFAs and consequently the formation of various eicosanoids. Some of these factors include: the ratio among various polyunsaturated fatty acids, antioxidants, phytochemicals, vitamins, minerals, hormones (especially estrogen, insulin, corticosteroids), gut microbiota, ethanol, oncogenic viruses, and genetics and age of the individual, and climactic temperature [57–62]. A brief description as to the way some of these factors influence EFA metabolism is given below (see also Figure 1).

Modulators of desaturases

It is well recognized that Δ^6 and Δ^5 desaturases are the rate-limiting factors in the production of long-chain metabolites of EFAs: LA and ALA [63–65]. Hence, factors that influence the activities of desaturases are expected to alter the tissue levels of LA and ALA and their long-chain metabolites. Thus, several nutritional, hormonal, and genetic factors are able to determine the plasma and tissue concentrations of various PUFAs as a result of their influence on the activity of desaturases [30, 66]. Δ^6 desaturase activity is upregulated by EFA, protein, insulin and dietary deficiency (calorie restriction), and downregulated by fasting, glucose, fructose, glycerol, EFA excess, metabolic hormones (other than insulin), ethanol and increasing age [29, 30, 57–66]. Δ^5 desaturase responds similarly to metabolic hormones, but in the event of EFA deficiency it is downregulated rapidly and is upregulated with increase in the activity of Δ^6 desaturase, showing a delayed response. On the other hand,

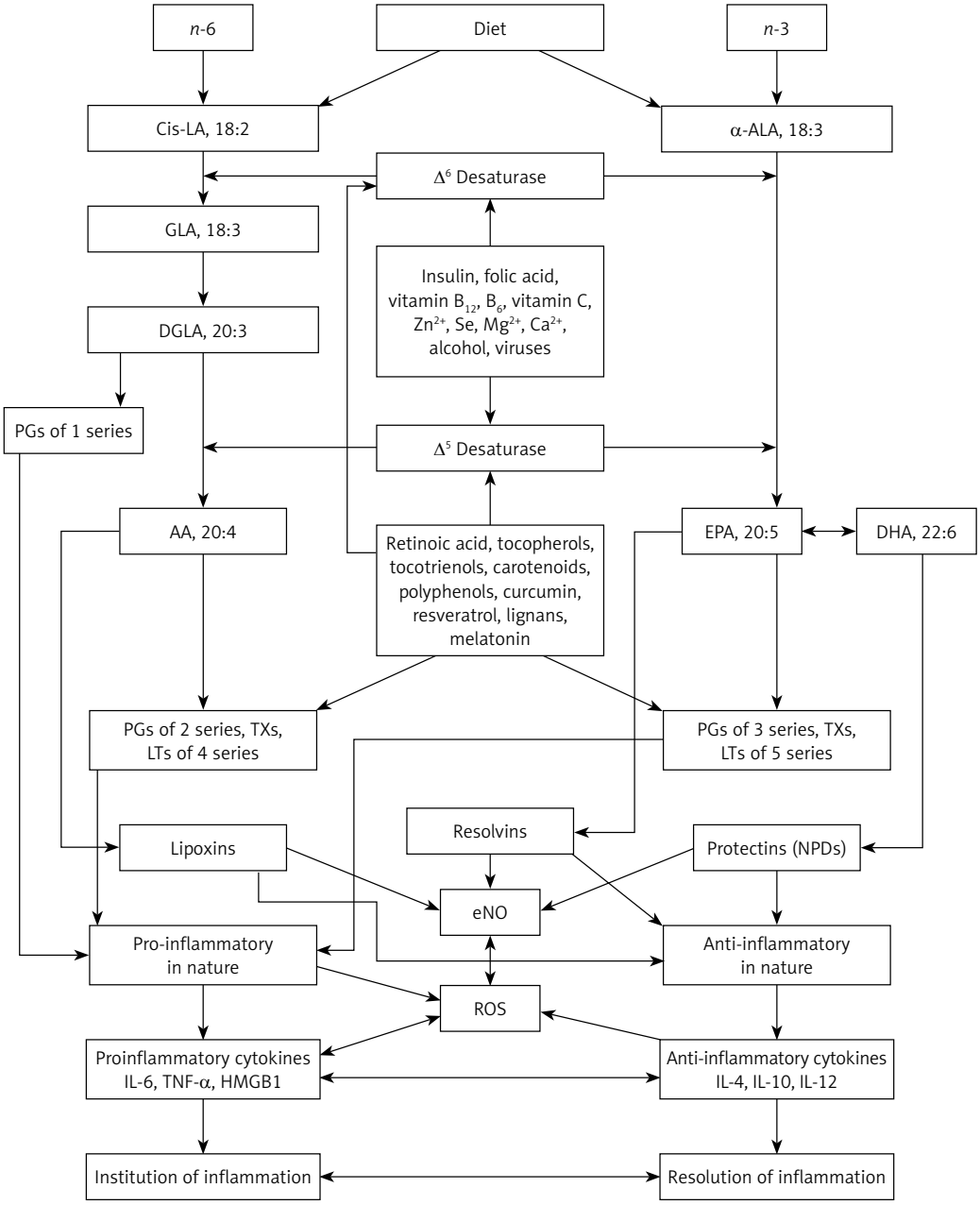

Figure 1. Scheme showing the metabolism of essential fatty acids, their role in inflammation and factors that influence desaturases

in response to an increase in EFA consumption (or increased release of EFAs from the cell membrane pool) the activity of Δ^6 desaturase declines whereas that of Δ^5 desaturase is increased [66, 67]. Once the feedback regulation comes into play, the activities of both the desaturases are restored to normal [30]. This may explain why a rapid increase in the consumption of ω-6 fatty acids by subjects who are deficient in these fatty acids (*n*-6 PUFAs) results in a sudden surge in the features of inflammation that could be attributed to increased formation of pro-inflammatory eicosanoids derived from *n*-6.

Males and females seem to differ in their ability to synthesize long-chain ω-3 fatty acids from ALA as a result of the action of estrogen and testosterone on its (ALA) metabolism. Estradiol increases, whereas testosterone decreases the production of long-chain metabolites derived from LA and ALA [20, 21]. It has been reported that the ω-3 pathway is more responsive to hormonal treatment than the ω-6 pathway; relatively low concentrations of estradiol increased the synthesis of EPA and docosapentaenoic acid (DPA) from ALA, but larger concentrations of estradiol were required to

increase the AA levels [68]. A lower partitioning of ALA for β-oxidation and a lower use as an energy source in women compared with men has also been reported, which may enhance its availability for the formation of EPA and DHA [69]. This could be one specific reason why greater DHA synthesis has been reported in women than men, which may result in higher plasma DHA concentration in women [70]. In females, the conversion from ALA to DHA may be as high as 9%, whereas for males it may be ~0.5–4% [70]. Growth hormones have been shown to increase the Δ^6 activity and consequently enhance the tissue levels of respective PUFAs in the tissues [71].

Vitamin A has been shown to downregulate the expression of Δ^5 [72]. In addition, some phytochemicals, particularly curcumin and sesamin, also downregulate Δ^5. But, surprisingly, both curcumin and sesamin suppressed desaturation of ω-6 fatty acids but not of ω-3 fatty acids [16, 73]. Curcumin is more effective than sesamin, while simultaneous use of both curcumin and sesamin had a greater suppressive effect on chain elongation, resulting in tissue accumulation of GLA and DGLA. In contrast, phytosterols enhanced the activity of Δ^6, Δ^5, and SCD [74]. Stearoyl CoA desaturase by virtue of its ability to introduce a double bond in SFA to form MUFA increases the unsaturation index and thus cell membrane fluidity (Figure 1).

The effect of temperature on the activity of desaturases has been controversial, some reporting an increase in Δ^6 activity at lower temperatures, while others report decreased activity [75–78]. It stands to reason to suggest that at low temperatures, the activity of desaturases could be higher, since to maintain cell membrane fluidity in a cold climate higher concentrations of unsaturated fatty acids are needed.

Arguably, one of the important factors that regulate the activity of desaturases is the cellular content of unsaturated fatty acids themselves. Under normal physiological conditions, cellular PUFA content is maintained within a narrow range by the activity of desaturases and elongases and their uptake and efflux. As expected, as is the case with the activity of many other enzymes in the cells, upregulation of the PUFA synthetic pathway occurs principally under conditions of deficiency while, as expected, downregulation of the desaturases and elongases occurs, rather quickly, once PUFAs have been replenished or provided [27, 67].

Other fatty acids

Although non-essential fatty acids can be synthesized endogenously, some of them are considered conditionally essential and they influence EFA metabolism. For example, OA not only has regulatory functions but can also alter cellular fatty acid composition in select organs [25]. Both saturated and unsaturated fatty acids are essential components of the cell membrane and contribute to many cellular functions as well. Some of these include: coordinating the expression of proteins involved in lipid synthesis, transport, storage, degradation, and elimination to maintain a normal physiological state [79, 80]. Several of these fatty acids function as ligands of nuclear and cell-surface receptors and thus maintain cellular homeostasis [26], by sensing cellular lipid levels and regulating gene expression to control lipid overload. The homeostatic role of lipids includes regulation of energy and glucose homeostasis through a feedback regulation between the gastrointestinal tract and central nervous system in which fatty acids with 12 or more carbons seem to have an important role by regulating food intake [81]. This sensitive neuronal circuitry becomes inefficient in response to high-fat or inappropriate fat intake, which could be attributed to imbalance in the ingestion of specific fatty acids [82]. Palmitic, lauric, and stearic acids stimulate the expression of mitochondrial uncoupling proteins, UCP2 and UCP3, which reduce oxidative stress and are known to play a role in determining longevity of the organism [83].

Dietary composition of fatty acids (including ω-6 and ω-3) is reflected in tissue composition [84, 85], which may have a modulatory influence on cellular functions. Similarly, the total amount of dietary fatty acids (low-fat versus high-fat diets) influences fatty acid metabolism and tissue composition. For instance, consumption of low fat diets seems to enhance plasma ω-3 fatty acid levels, which could be due to the preferential metabolism of ALA [86]. Increased intake of a high fat diet, especially saturated fats, can be a risk factor for the development of hypertension [4]. Whether this increase in blood pressure due to high intake of saturated fats may be related to interference with the metabolism of essential fatty acids and/or an imbalance in the formation of their eicosanoid metabolites remains to be established. Nevertheless, it is likely that the proportion of ω-6 and ω-3 fatty acids, saturated fats and concomitant consumption of total protein and carbohydrate may all play a significant role in the pathobiology of hypertension and other cardiovascular diseases [87–92].

Antioxidants, phytochemicals, vitamins and minerals

Following the ingestion of fatty acids, they may undergo: (1) mitochondrial and peroxisomal β-oxidation for energy production, (2) free-radical mediated oxidation (chain reactions where one free radical can oxidize many lipid molecules), (3) free-radical independent, non-enzymatic oxi-

dation, and/or (4) enzymatic oxidation to produce bioactive lipid products including long-chain fatty acids and various eicosanoids. Specific products are formed from each type of oxidation and specific antioxidants are known to modulate specific reaction [9, 93]. This may explain the regulatory or modulatory role played by several antioxidants, phytochemicals, vitamins, and minerals in the metabolism or bioavailability of various fatty acids.

Vitamin E and C work synergistically to prevent lipid peroxidation [9, 94]. Both cyclooxygenase-2 (COX-2) activity and lipid peroxidation increase with age, which could be inhibited by vitamin E [95–100]. PGE2, a product of COX-2 activity, is an immunosuppressor and so it is anticipated that vitamin E may be able to restore immune dysfunction and increase T-cell-mediated immune function [98, 99]. γ-Tocopherol (γT) is a more effective inhibitor of PGE_2, LTB_4, and tumor necrosis factor-α (TNF-α) than α-tocopherol (αT) [100]. It is worth noting that with advancing age, production of pro-inflammatory cytokines IL-6 and TNF-α increases, while both vitamin E and PUFAs and their eicosanoid products inhibit their (IL-6 and TNF-α) synthesis [98–102]. On the other hand, increased production of free radicals and the lipid peroxidation process, which increase with aging, may have an impact on the availability of PUFAs, since the latter are easily peroxidized. Thus, there appears to be close but intricate and complex interaction among vitamin E, PUFAs, eicosanoids, lipid peroxidation and cytokines that ultimately may impact the immune response and various aging associated diseases such as type 2 diabetes mellitus, hypertension, metabolic syndrome, Alzheimer's disease and cancer. Thus, vitamin E requirements are partially dependent on PUFA consumption, partly because PUFAs reduce intestinal absorption of vitamin E [10]. In this context, it is important to note that the results of the GISSI trial [103] reported that vitamin E supplementation does not prevent myocardial infarction and yet other studies showed that both β-carotenoids and vitamin A intake may actually increase the incidence of cancer in the high-risk population [104]. These results suggest that the timing, dose, and form of administration of anti-oxidants may produce unexpected and contradictory results. Studies have also shown that vitamin A can modulate PUFA metabolism and formation of various eicosanoids [105, 106]. Folic acid stimulates the formation of long-chain *n*-3 fatty acids [107], which may explain its importance in brain growth and function for which even PUFAs are essential.

Phytochemicals stimulate the synthesis of detoxifying and antioxidant enzymes and may also modulate plasma membrane structure and act as ligands to certain cellular signaling molecules [13, 108–110]. For instance, curcumin accumulates in the plasma membrane and alters thickness, fluidity, and elasticity, whereas resveratrol increases membrane fluidity [13].

Melatonin, the circadian rhythm regulator, has the ability to counteract lipid peroxidation in biological membranes and serve as an antioxidant [111]. Long-term melatonin administration reduced hyperinsulinemia and improved the altered fatty-acid compositions in type 2 diabetic rats via the restoration of Δ^5 activity, indicating that melatonin can modulate essential fatty acid metabolism [112].

The influence of minerals and trace elements on AA metabolism and eicosanoid production is complex [19]. Selenium, an important component of the Se-dependent enzyme glutathione peroxidase (Se-GSHpx), functions synergistically with vitamin E as an antioxidant and thus may prevent lipid peroxidation and alter the production of eicosanoids. Zinc, cadmium, silver, iron, and mercury are inhibitors of Se-GSHpx, which is known to catalyze AA metabolism to form PGs, TXs, and LTs. Free radical generated during the formation of various eicosanoids themselves may have a feedback regulatory function on their (eicosanoids) formation [113–115]. Thus, while considering the metabolism of PUFAs and the formation of various eicosanoids, one needs to take into account the presence, actions and concentrations of various antioxidants, phytochemicals, vitamins, and minerals.

The biological role of lipid peroxides is complex, especially with regard to their role in pathological processes and diseases such as diabetes, atherosclerosis, inflammation, aging, and ischemia-reperfusion injury [9, 96]. It is believed that low to moderate levels of lipid peroxides are essential for cellular functions by triggering adaptive responses that are necessary to prevent cytotoxic actions of oxidative stress by upregulating protective antioxidant defenses [9, 60, 61, 113–115].

Gut microbiota

Gut microflora can influence lipogenesis and plasma lipopolysaccharide levels [116]. A high-fat diet may have an unfavorable effect on gut microflora [117], while the gut microbiota influences fat composition of host tissue. For instance, administration of *Bifidobacterium breve* with linoleic acid increased the tissue composition of conjugated-linoleic acid and ω-3 fatty acids EPA and DHA [118]. The effect of other PUFAs on gut microbiota remains to be determined.

Gender, genetics and aging

Sex hormones can alter metabolism of dietary fats [20, 21], while dietary fats modulate the syn-

thesis of sex hormones and the associated receptor organization [99, 119]. Higher PUFA administration resulted in lower activity of steroidogenic enzymes and low levels of androgens as compared to MUFA or SFA administration. ω-3 fatty acids, particularly DHA, caused less androgen production than ω-6 fatty acids; and ω-6 fatty acids caused less androgen production than MUFA or SFA (ω-3 > ω-6 > MUFA = SFA) [120]. For this alteration in the androgen levels to occur, fatty acids need to be administered for at least 3 weeks, while feeding fats for 6 weeks led to a decrease in androgen, implying that adapter mechanisms come into play when fats are fed for longer periods [121]. A similar relationship that has been shown by androgen production seems to exist between estrogen and PUFAs [122]. Both estrogen and PUFAs enhance nitric oxide synthesis, suppress the production of pro-inflammatory IL-6 and TNF-α production and have antioxidant-like and anti-atherosclerotic properties, and showed neuroprotective actions [122]. Men and women differ in storage, mobilization, and oxidation of fatty acids [123, 124], and gene expression relevant to fatty acid metabolism [125–127].

Genetic variations in the activity of delta desaturases and elongases can influence metabolism and therefore the requirement and concentrations of cellular lipids [23]. Similarly, polymorphisms in apolipoprotein E and peroxisome-proliferator-activated receptor-γ (PPAR-γ) genes alter the response to dietary fats [126]. On the other hand, dietary fats can alter the expression of several genes. For instance, PUFAs suppress lipogenic, glycolytic, and cholesterologenic genes, but enhance the expression of genes of the β-oxidation pathway [127, 128]. The PUFAs modulate gene expression by interacting with nuclear receptors – hepatic nuclear factor (HNF-4), liver X receptors (LXR), and PPAR α, β, δ, and γ – and by regulating transcription factor sterol regulatory element-binding proteins (SREBP) 1 and 2 [128]. SREBPs, suppressed by PUFAs, are key regulators of cholesterol, fatty acid, and triglyceride synthesis. Linoleic acid and AA are potent PPAR ligands, producing a rapid increase in expression of genes involved in lipid oxidation.

Phytochemicals bind to the cell surface and nuclear receptors as ligands. Curcumin, capsaicin, ginsenosides, hesperidin, and resveratrol are PPAR-γ ligands, attenuate cytokine production and thus suppress inflammation [18]. Phytosterols alter expression of intestinal and hepatic genes [129]. Since nutrients are able to alter a variety of genes, it is tempting to suggest that fine tuning of the ingestion of various nutritional factors could be employed to optimize gene expression and thus prevent several diseases.

It is believed that with advancing age membrane fluidity declines, lipid peroxidation increases and so also does oxidative stress. Aging is one of the factors that impact the activity of desaturases, leading to an alteration in the formation of long-chain metabolites of EFAs: LA and ALA. Thus, this could be a compensatory phenomenon – as oxidative stress increases with age, the activity of desaturases changes and the tissues try to maintain near normal amounts of PUFA though they could form substrates for the peroxidation process. But, this delicate balance between oxidative stress and peroxidation on one hand and the activity of desaturases on the other hand may lead to significant alterations in cell membrane fluidity, formation of various eicosanoids, and consequently changes in the formation of cytokines – events that could have a profound influence on the immune response and inflammation. Calorie restriction enhances the activity of desaturases, which could be considered as yet another compensatory phenomenon since with aging food intake decreases. Since calorie restriction also extends life span, it is tempting to suggest that the close interaction(s) among oxidative stress of aging, lipid peroxidation, activity of desaturases, formation of various eicosanoids, calorie intake, production of cytokines and consequent alterations in inflammation and immunity may be relevant to the involvement of these changes in a variety of diseases.

It has been suggested that a decline in brain DHA content with age is associated with increased lipid peroxidation [130] that may lead to impaired cognitive function as a result of neuronal apoptosis of the cerebral cortex and hippocampus [131]. Hence, increased consumption of DHA (in the form of fish oil) could be of benefit in dementia of aging, Alzheimer's disease and depression. This suggestion looks paradoxical since one would expect that increased consumption of DHA may enhance the lipid peroxidation process and enhance oxidative stress. But, in practice enhanced DHA consumption failed to increase oxidative stress in humans [132, 133], implying that the lipid peroxidation process does not just depend on the amount of unsaturation and is not a non-specific process but could be a specific enzymatic process that depends on local cellular integrity, function, and the necessity of eicosanoids and other products for various physiological and pathological processes.

Conclusions

It is evident from the preceding discussion that PUFAs not only form an important constituent of the cell membrane but also play an important role in inflammation and immunity. The effect of PUFAs on

inflammation and immunity depends on the products formed from them. The exact mechanisms that determine what types of products are derived from various PUFAs – pro-inflammatory or anti-inflammatory – is not clear. Both PUFAs and the products formed from these fatty acids may ultimately determine the initiation, continuation and/or resolution of inflammation and the magnitude and type of immune response [134]. Some, if not all, of the actions of PUFAs and their products on inflammation and immunity could be attributed to their action on NF-κB, PPARs and other transcription factors.

Though it is not yet certain, it is likely that cellular stores of PUFAs and phytochemicals and other co-factors that alter fatty acid and eicosanoid metabolism play a significant role in several disease processes. It is possible that a sudden withdrawal of or alteration in the proportion of intake of different types of PUFAs may result in a sudden surge in the production or inhibition of certain eicosanoids that may result in unrestrained or significant alterations in production/suppression of cytokines and gene(s) expression that may result in significant alterations in the physiological or pathological processes including changes in LDL, HDL and cholesterol [135–137]. Such sudden and, sometimes, even gradual and unanticipated changes in the concentrations of various PUFAs, eicosanoids, cytokines, oxidative stress, HDL (may make HDL dysfunctional), LDL, cholesterol, triglycerides and other bioactive molecules may render the host vulnerable to infections, myocardial infarction, stroke, and other diseases and their complications [138–157].

In view of this, it is essential to determine the individual necessity of various monounsaturated, ω-6, ω-3 and other fatty acids, antioxidants, and phytochemicals and administer them accordingly. Such an individualized approach may be more fruitful in tackling several diseases in which PUFAs are believed to play a significant role. Development of such personalized dietary lipid programs for different types of subjects depending on their age, gender, dietary practices, environmental factors (such as temperature, season, etc.), hormonal status, stress and strain of life and other life style factors (such as exercise, etc.) and genetic background is probably necessary and important to derive the best out of PUFAs, phytochemicals, vitamins and other co-factors for optimum health and to ward off diseases.

In this context, it is noteworthy that some of the beneficial actions of statins could be brought about by PUFAs [158] and implies that a combination of statins and PUFAs may be more beneficial to patients with hyperlipidemias including those who have statin intolerance [159].

Such a dietary program should also take into consideration the necessity of saturated, monounsaturated, and polyunsaturated fatty acids, phytochemicals, antioxidants, and minerals, such that the body tissues would have access to all the required raw chemicals/ingredients to form the beneficial bioactive compounds to optimize health.

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Conflict of interest

Urvashi Bhagat is CEO of Asha Nutrition; Undurti N. Das is the Chief Medical Officer and Chairman of the Scientific Advisory Board of Asha Nutrition. Asha Nutrition has developed and marketed products based on essential fatty acids and other fatty acids.

References

1. Galli C, Calder PC. Effects of fat and fatty acid intake on inflammatory and immune responses: a critical review. Ann Nutr Metab 2009; 55: 123-39.
2. Simopoulos AP. n-3 fatty acids and human health: defining strategies for public policy. Lipids 2001; 36 Suppl: S83-9.
3. Hodge AM, English DR, O'Dea K, et al. Plasma phospholipid and dietary fatty acids as predictors of type 2 diabetes: interpreting the role of linoleic acid. Am J Clin Nutr 2007; 86: 189-97.
4. Rasmussen BM, Vessby B, Uusitupa M, et al. Effects of dietary saturated, monounsaturated, and n-3 fatty acids on blood pressure in healthy subjects. Am J Clin Nutr 2006; 83: 221-6.
5. Das UN. Molecular basis of health and disease. Springer, New York 2011.
6. DeLany JP, West DB. Changes in body composition with conjugated linoleic acid. J Am Coll Nutr 2000; 19: 487S-93S.
7. Kapoor R, Huang YS. Gamma linolenic acid: an antiinflammatory omega-6 fatty acid. Curr Pharm Biotechnol 2006; 7: 531-4.
8. Ramsden CE, Zamora D, Leelarthaepin B, et al. Use of dietary linoleic acid for secondary prevention of coronary heart disease and death: evaluation of recovered data from the Sydney Diet Heart Study and updated meta-analysis. Br Med J 2013; 346: e8707.
9. Niki E. Lipid peroxidation: physiological levels and dual biological effects. Free Radic Biol Med 2009; 47: 469-84.
10. Bassler KH. On the problematic nature of vitamin E requirements: net vitamin E. Z Ernahrungswiss 1991; 30: 174-80.
11. Meydani SN, Barklund MP, Liu S, et al. Vitamin E supplementation enhances cell-mediated immunity in healthy elderly subjects. Am J Clin Nutr 1990; 52: 557-63.
12. Sujak A, Gabrielska J, Grudzinski W, Borc R, Mazurek P, Gruszecki WI. Lutein and zeaxanthin as protectors of lipid membranes against oxidative damage: the structural aspects. Arch Biochem Biophys 1999; 371: 301-7.

13. Ding H, Tauzin S, Hoessli DC. Phytochemicals as modulators of neoplastic phenotypes. Pathobiology 2009; 76: 55-63.
14. Terao J, Kawai Y, Murota K. Vegetable flavonoids and cardiovascular disease. Asia Pac J Clin Nutr 2008; 17 Suppl 1: 291-3.
15. O'Leary KA, de Pascual-Tereasa S, Needs PW, Bao YP, O'Brien NM, Williamson G. Effect of flavonoids and vitamin E on cyclooxygenase-2 (COX-2) transcription. Mutat Res 2004; 551: 245-54.
16. Fujiyama-Fujiwara Y, Umeda R, Igarashi O. Effects of sesamin and curcumin on delta 5-desaturation and chain elongation of polyunsaturated fatty acid metabolism in primary cultured rat hepatocytes. J Nutr Sci Vitaminol (Tokyo)1992; 38: 353-63.
17. Shah BH, Nawaz Z, Pertani SA, et al. Inhibitory effect of curcumin, a food spice from turmeric, on platelet-activating factor- and arachidonic acid-mediated platelet aggregation through inhibition of thromboxane formation and Ca2+ signaling. Biochem Pharmacol 1999; 58: 1167-72.
18. Marion-Letellier R, Dechelotte P, Iacucci M, Ghosh S. Dietary modulation of peroxisome proliferator-activated receptor gamma. Gut 2009; 58: 586-93.
19. Peplow PV. Modification to dietary intake of sodium, potassium, calcium, magnesium and trace elements can influence arachidonic acid metabolism and eicosanoid production. Prostaglandins Leukot Essent Fatty Acids 1992; 45: 1-19.
20. Giltay EJ, Gooren LJ, Toorians AW, Katan MB, Zock PL. Docosahexaenoic acid concentrations are higher in women than in men because of estrogenic effects. Am J Clin Nutr 2004; 80: 1167-74.
21. Hurtado de Catalfo GE, de Gomez Dumm IN. Influence of testosterone on polyunsaturated fatty acid biosynthesis in Sertoli cells in culture. Cell Biochem Funct 2005; 23: 175-80.
22. Hulbert AJ, Pamplona R, Buffenstein R, Buttemer WA. Life and death: metabolic rate, membrane composition, and life span of animals. Physiol Rev 2007; 87: 1175-213.
23. Ordovas JM, Mooser V. Nutrigenomics and nutrigenetics. Curr Opin Lipidol 2004; 15: 101-8.
24. Ratnayake WM, Galli C. Fat and fatty acid terminology, methods of analysis and fat digestion and metabolism: a background review paper. Ann Nutr Metab 2009; 55: 8-43.
25. Bourre JM, Dumont O, Durand G. Dose-effect of dietary oleic acid: oleic acid is conditionally essential for some organs. Reprod Nutr Dev 2004; 44: 371-80.
26. Hirasawa A, Hara T, Katsuma S, Adachi T, Tsujimoto G. Free fatty acid receptors and drug discovery. Biol Pharm Bull 2008; 31: 1847-51.
27. Nakamura MT, Cho HP, Xu J, Tang Z, Clarke SD. Metabolism and functions of highly unsaturated fatty acids: an update. Lipids 2001; 36: 961-4.
28. Calder PC. Polyunsaturated fatty acids and inflammatory processes: new twists in an old tale. Biochimie 2009; 91: 791-5.
29. Brenner RR. The oxidative desaturation of unsaturated fatty acids in animals. Mol Cell Biochem 1974; 3: 41-52.
30. Nakamura MT, Nara TY. Structure, function, and dietary regulation of delta6, delta5, and delta9 desaturases. Annu Rev Nutr 2004; 24: 345-76.
31. Brenner RR, Peluffo RO. Effect of saturated and unsaturated fatty acids on the desaturation in vitro of palmitic, stearic, oleic, linoleic, and linolenic acids. J Biol Chem 1966; 241: 5213-9.
32. Holman RT. The slow discovery of the importance of omega 3 essential fatty acids in human health. J Nutr 1998; 128 (2 Suppl): 427S-33S.
33. Simopoulos AP. Evolutionary aspects of diet, the omega-6/omega-3 ratio and genetic variation: nutritional implications for chronic diseases. Biomed Pharmacother 2006; 60: 502-7.
34. Yehuda S, Carasso RL. Modulation of learning, pain thresholds, and thermoregulation in the rat by preparations of free purified alpha-linolenic and linoleic acids: determination of the optimal omega 3-to-omega 6 ratio. Proc Natl Acad Sci U S A 1993; 90: 10345-9.
35. Rapoport SI, Rao JS, Igarashi M. Brain metabolism of nutritionally essential polyunsaturated fatty acids depends on both the diet and the liver. Prostaglandins Leukot Essent Fatty Acids 2007; 77: 251-61.
36. Morse NL. A meta-analysis of blood fatty acids in people with learning disorders with particular interest in arachidonic acid. Prostaglandins Leukot Essent Fatty Acids 2009; 81: 373-89.
37. Nassar BA, Huang YS, Manku MS, Das UN, Morse N, Horrobin DF. The influence of dietary manipulation with n-3 and n-6 fatty acids on liver and plasma phospholipid fatty acids in rats. Lipids 1986; 21: 652-6.
38. Wang L, Folsom AR, Zheng ZJ, Pankow JS, Eckfeldt JH. Plasma fatty acid composition and incidence of diabetes in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. Am J Clin Nutr 2003; 78: 91-8.
39. Vessby B, Aro A, Skarfors E, Berglund L, Salminen I, Lithell H. The risk to develop NIDDM is related to the fatty acid composition of the serum cholesterol esters. Diabetes 1994; 43: 1353-7.
40. Ohrvall M, Berglund L, Salminen I, Lithell H, Aro A, Vessby B. The serum cholesterol ester fatty acid composition but not the serum concentration of alpha tocopherol predicts the development of myocardial infarction in 50-year-old men: 19 years follow-up. Atherosclerosis 1996; 127: 65-71.
41. Miettinen TA, Naukkarinen V, Huttunen JK, Mattila S, Kumlin T. Fatty-acid composition of serum lipids predicts myocardial infarction. Br Med J (Clin Res Ed) 1982; 285: 993-6.
42. Wiberg B, Sundstrom J, Arnlov J, et al. Metabolic risk factors for stroke and transient ischemic attacks in middle-aged men: a community-based study with long-term follow-up. Stroke 2006; 37: 2898-903.
43. Sundstrom J, Lind L, Vessby B, Andren B, Aro A, Lithell H. Dyslipidemia and an unfavorable fatty acid profile predict left ventricular hypertrophy 20 years later. Circulation 2001; 103: 836-41.
44. Vessby B, Gustafsson IB, Tengblad S, Boberg M, Andersson A. Desaturation and elongation of fatty acids and insulin action. Ann N Y Acad Sci 2002; 967: 183-95.
45. Warensjo E, Riserus U, Vessby B. Fatty acid composition of serum lipids predicts the development of the metabolic syndrome in men. Diabetologia 2005; 48: 1999-2005.
46. Petersson H, Basu S, Cederholm T, Riserus U. Serum fatty acid composition and indices of stearoyl-CoA desaturase activity are associated with systemic inflammation: longitudinal analyses in middle-aged men. Br J Nutr 2008; 99: 1186-9.
47. Warensjo E, Sundstrom J, Vessby B, Cederholm T, Riserus U. Markers of dietary fat quality and fatty acid desaturation as predictors of total and cardiovascular mortality: a population-based prospective study. Am J Clin Nutr 2008; 88: 203-9.

48. Das UN. A defect in the activity of Delta6 and Delta5 desaturases may be a factor in the initiation and progression of atherosclerosis. Prostaglandins Leukot Essent Fatty Acids 2007; 76: 251-68.
49. Das UN. A defect in the activity of delta6 and delta5 desaturases may be a factor predisposing to the development of insulin resistance syndrome. Prostaglandins Leukotrienes Essen Fatty Acids 2005; 72: 343-50.
50. Kahn SG, Wind S, Slocum A, Pfeffer D, Yacowitz H. A study of the hypocholesterolemic activity of the ethyl esters of the polyunsaturated fatty acids of cod liver oil in the chicken. II. Effect on serum and tissue cholesterol and aortic and coronary atherosclerosis. J Nutr 1963; 80: 414-24.
51. Kahn SG, Vandeputte J, Wind S, Yacowitz AD. A Study of the hypocholesterolemic activity of the ethyl esters of the polyunsaturated fatty acids of cod liver oil in the chicken. I. Effect on total cholesterol. J Nutr 1963; 80: 403-13.
52. Kahn SG. A study of the hypocholesterolemic activity of the ethyl esters of the polyunsaturated fatty acids of cod liver oil in the rat. J Nutr 1964; 83: 262-6.
53. Kingsbury KJ, Aylott C, Morgan DM, Emmerson R. Effects of ethyl arachidonate, cod-liver oil, and corn oil on the plasma-cholesterol level. A comparison in normal volunters. Lancet 1961; 1: 739-41.
54. De Groot AP, Reed SA. Influence of dietary cod-liver oil and some fractions of cod-liver oil on serum cholesterol-level of rats. Nature 1959; 183: 1191.
55. Hauge JG, Nicolaysen R. The serum cholesterol depressive effect of linoleic, linolenic acids and of cod liver oil in experimental hypercholesterolaemic rats. Acta Physiol Scand 1959; 45: 26-30.
56. Dasgupta S, Bhattacharyya DK. Dietary effect of gamma-linolenic acid on the lipid profile of rat fed erucic acid rich oil. J Oleo Sci 2007; 56: 569-77.
57. Das UN. Hemostatic vitamins and prostaglandins. Med J Australia 1982; 2: 316.
58. Das UN. Minerals, trace elements and vitamins interact with essential fatty acids and prostaglandins to prevent hypertension, thrombosis, hypercholesterolemia and atherosclerosis and their attendant complications. IRCS J Med Sci 1985; 13: 684-6.
59. Huang YS, Das UN Horrobin DF. Effect of dexamethasone on the distribution of essential fatty acids in plasma and liver phospholipids. IRCS Med Sci 1986; 14: 180-1.
60. Das UN. Metabolic syndrome pathophysiology: the role of essential fatty acids and their metabolites. Wiley-Blackwell Publishers, Ames, IA, USA, 2010.
61. Das UN. Molecular basis of health and disease. Springer, New York 2011.
62. Das UN. Folic acid and polyunsaturated fatty acids improve cognitive function and prevent depression, dementia, and Alzheimer's disease: but how and why? Prostaglandins Leukot Essent Fatty Acids 2008; 78: 11-9.
63. Das UN. Delta6 desaturase as the target of the beneficial actions of magnesium. Med Sci Monit 2010; 16: LE11-2.
64. Das UN. Essential fatty acids – a review. Curr Pharmaceut Biotechnol 2006; 7: 467-82.
65. Das UN. Essential fatty acids: biochemistry, physiology, and pathology. Biotechnol J 2006; 1: 420-39.
66. Brenner RR. Nutritional and hormonal factors influencing desaturation of essential fatty acids. Prog Lipid Res 1981; 20: 41-7.
67. Le HD, Fallon EM, Kalish BT, et al. The effect of varying ratios of docosahexaenoic acid and arachidonic acid in the prevention and reversal of biochemical essential fatty acid deficiency in a murine model. Metabolism 2013; 62: 499-508.
68. Extier A, Perruchot MH, Baudry C, Guesnet P, Lavialle M, Alessandri JM. Differential effects of steroids on the synthesis of polyunsaturated fatty acids by human neuroblastoma cells. Neurochem Int 2009; 55: 295-301.
69. Burdge G. Alpha-linolenic acid metabolism in men and women: nutritional and biological implications. Curr Opin Clin Nutr Metab Care 2004; 7: 137-44.
70. Bakewell L, Burdge GC, Calder PC. Polyunsaturated fatty acid concentrations in young men and women consuming their habitual diets. Br J Nutr 2006; 96: 93-9.
71. Nakamura MT, Phinney SD, Tang AB, Oberbauer AM, German JB, Murray JD. Increased hepatic delta 6-desaturase activity with growth hormone expression in the MG101 transgenic mouse. Lipids 1996; 31: 139-43.
72. Zolfaghari R, Cifelli CJ, Banta MD, Ross AC. Fatty acid delta(5)-desaturase mRNA is regulated by dietary vitamin A and exogenous retinoic acid in liver of adult rats. Arch Biochem Biophys 2001; 391: 8-15.
73. Shimizu S, Akimoto K, Shinmen Y, Kawashima H, Sugano M, Yamada H. Sesamin is a potent and specific inhibitor of delta 5 desaturase in polyunsaturated fatty acid biosynthesis. Lipids 1991; 26: 512-6.
74. Leikin AI, Brenner RR. Fatty acid desaturase activities are modulated by phytosterol incorporation in microsomes. Biochim Biophys Acta 1989; 1005: 187-91.
75. Ves Losada A, Peluffo RO. Effect of cold environment on hepatic microsomal delta 6 and delta 9 desaturase activity of male rats. Lipids 1987; 22: 583-8.
76. Gonzalez S, Nervi AM, Peluffo RO, Brenner RR. Effect of environmental temperature changes on rat liver fatty acid desaturases. Lipids 1983; 18: 7-11.
77. Brodte E, Graeve M, Jacob U, Knust R, Pörtner HO. Temperature-dependent lipid levels and components in polar and temperate eelpout (Zoarcidae). Fish Physiol Biochem 2008; 34: 261-74.
78. Dinh TK, Bourre JM, Durand G. Effect of age and alpha-linolenic acid deficiency on delta 6 desaturase activity and liver lipids in rats. Lipids 1993; 28: 517-23.
79. Cho HP, Nakamura M, Clarke SD. Cloning, expression, and fatty acid regulation of the human delta-5 desaturase. J Biol Chem 1999; 274: 37335-9.
80. Chawla A, Repa JJ, Evans RM, Mangelsdorf DJ. Nuclear receptors and lipid physiology: opening the X-files. Science 2001; 294: 1866-70.
81. Cheung GW, Kokorovic A, Lam TK. Upper intestinal lipids regulate energy and glucose homeostasis. Cell Mol Life Sci 2009; 66: 3023-7.
82. Lam CK, Chari M, Lam TK. CNS regulation of glucose homeostasis. Physiology (Bethesda) 2009; 24: 159-70.
83. Kua CH. Uncoupling the relationship between fatty acids and longevity. IUBMB Life 2006; 58: 153-5.
84. Dougherty RM, Galli C, Ferro-Luzzi A, Iacono JM. Lipid and phospholipid fatty acid composition of plasma, red blood cells, and platelets and how they are affected by dietary lipids: a study of normal subjects from Italy, Finland, and the USA. Am J Clin Nutr 1987; 45: 443-55.
85. Andersson A, Nalsen C, Tengblad S, Vessby B. Fatty acid composition of skeletal muscle reflects dietary fat composition in humans. Am J Clin Nutr 2002; 76: 1222-9.
86. Raatz SK, Bibus D, Thomas W, Kris-Etherton P. Total fat intake modifies plasma fatty acid composition in humans. J Nutr 2001; 131: 231-4.

87. Das UN. Essential fatty acids and their metabolites in the context of hypertension. Hypertension Res 2010; 33: 782-5.
88. Weisinger HS, Armitage JA, Sinclair AJ, Vingrys AJ, Burns PL, Weisinger RS. Perinatal omega-3 fatty acid deficiency affects blood pressure later in life. Nat Med 2001; 7: 258-9.
89. Begg DP, Sinclair AJ, Stahl LA, et al. Hypertension induced by omega-3 polyunsaturated fatty acid deficiency is alleviated by alpha-linolenic acid regardless of dietary source. Hypertens Res 2010; 33: 808-13.
90. Suryaprabha P, Das UN, Koratkar R, Sangeetha P, Ramesh G. Free radical generation, lipid peroxidation and essential fatty acids in uncontrolled hypertension. Prostaglandins Leukot Essen Fatty Acids 1990; 41: 27-33.
91. Das UN. Essential fatty acids and their metabolites could function as endogenous HMG-CoA reductase and ACE enzyme inhibitors, anti-arrhythmic, anti-hypertensive, anti-atherosclerotic, anti-inflammatory, cytoprotective, and cardioprotective molecules. Lipids Health Dis 2008; 7: 37.
92. Das UN. Interaction(s) of polyunsaturated fatty acids with dietary protein and its relationship to the pathogenesis of hypertension. Am J Hypertens 2010; 23: 111-2.
93. Buettner GR. The pecking order of free radicals and antioxidants: lipid peroxidation, alpha-tocopherol, and ascorbate. Arch Biochem Biophys 1993; 300: 535-43.
94. Turchetto E, Pignatti C. Protection of essential fatty acids by vitamin E. Acta Vitaminol Enzymol 1982; 4: 267-77.
95. Cabré E, Periago JL, Mingorance MD, et al. Factors related to the plasma fatty acid profile in healthy subjects, with special reference to antioxidant micronutrient status: a multivariate analysis. Am J Clin Nutr 1992; 55: 831-7.
96. Yilmaz O, Celik S, Naziroğlu M, Cay M, Dilsiz N. The effects of dietary selenium and vitamin E and their combination on the fatty acids of erythrocytes, bone marrow and spleen tissue lipids of lambs. Cell Biochem Funct 1997; 15: 1-7.
97. Meydani SN, Meydani M, Verdon CP, Shapiro AA, Blumberg JB, Hayes KC. Vitamin E supplementation suppresses prostaglandin E1(2) synthesis and enhances the immune response of aged mice. Mech Ageing Dev 1986; 34: 191-201.
98. Wu D, Mura C, Beharka AA, et al. Age-associated increase in PGE2 synthesis and COX activity in murine macrophages is reversed by vitamin E. Am J Physiol 1998; 275: C661-8.
99. Meydani SN, Wu D. Nutrition and age-associated inflammation: implications for disease prevention. JPEN J Parenter Enteral Nutr 2008; 32: 626-9.
100. Jiang Q, Ames BN. Gamma-tocopherol, but not alpha-tocopherol, decreases proinflammatory eicosanoids and inflammation damage in rats. FASEB J 2003; 17: 816-22.
101. Sravan Kumar G, Das UN, Vijay Kumar K, Madhavi, Das NP, Tan BKH. Effect of n-6 and n-3 fatty acids on the proliferation and secretion of TNF and IL-2 by human lymphocytes in vitro. Nutrition Res 1992; 12: 815-23.
102. Sravan Kumar G, Das UN. Effect of prostaglandins and their precursors on the proliferation of human lymphocytes and their secretion of tumor necrosis factor and various interleukins. Prostaglandins Leukotrienes Essential Fatty Acids 1994; 50: 331-4.
103. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico. Lancet 1999; 354: 447-55.
104. Omenn GS. Chemoprevention of lung cancer: the rise and demise of beta-carotene. Annu Rev Public Health 1998; 19: 73-99.
105. Kampmann E, Johann S, van Neerven S, Beyer C, Mey J. Anti-inflammatory effect of retinoic acid on prostaglandin synthesis in cultured cortical astrocytes. J Neurochem 2008; 106: 320-32.
106. Hung LF, Lai JH, Lin LC, et al. Retinoid acid inhibits IL-1-induced iNOS, COX-2 and chemokine production in human chondrocytes. Immunol Invest 2008; 37: 675-93.
107. Pita ML, Delgado MJ. Folate administration increases n-3 polyunsaturated fatty acids in rat plasma and tissue lipids. Thromb Haemost 2000; 84: 420-3.
108. Candelario-Jalil E, de Oliveira AC, Graf S, et al. Resveratrol potently reduces prostaglandin E2 production and free radical formation in lipopolysaccharide-activated primary rat microglia. J Neuroinflammation 2007; 4: 25.
109. Bouhamidi R, Prevost V, Nouvelot A. High protection by grape seed proanthocyanidins (GSPC) of polyunsaturated fatty acids against UV-C induced peroxidation. C R Acad Sci III 1998; 321: 31-8.
110. Nonaka M, Yamashita K, Iizuka Y, Namiki M, Sugano M. Effects of dietary sesaminol and sesamin on eicosanoid production and immunoglobulin level in rats given ethanol. Biosci Biotechnol Biochem 1997; 61: 836-9.
111. Catala A. The ability of melatonin to counteract lipid peroxidation in biological membranes. Curr Mol Med 2007; 7: 638-49.
112. Nishida S, Segawa T, Murai I, Nakagawa S. Long-term melatonin administration reduces hyperinsulinemia and improves the altered fatty-acid compositions in type 2 diabetic rats via the restoration of Delta-5 desaturase activity. J Pineal Res 2002; 32: 26-33.
113. Droge W. Free radicals in the physiological control of cell function. Physiol Rev 2002; 82: 47-95.
114. Spahis S, Vanasse M, Belanger SA, Ghadirian P, Grenier E, Levy E. Lipid profile, fatty acid composition and pro- and anti-oxidant status in pediatric patients with attention-deficit/hyperactivity disorder. Prostaglandins Leukot Essent Fatty Acids 2008; 79: 47-53.
115. Levy E, Rizwan Y, Thibault L, et al. Altered lipid profile, lipoprotein composition, and oxidant and antioxidant status in pediatric Crohn disease. Am J Clin Nutr 2000; 71: 807-15.
116. Cani PD, Delzenne NM. Gut microflora as a target for energy and metabolic homeostasis. Curr Opin Clin Nutr Metab Care 2007; 10: 729-34.
117. Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. An obesity-associated gut microbiome with increased capacity for energy harvest. Nature 2006; 444: 1027-31.
118. Wall R, Ross RP, Shanahan F, et al. Metabolic activity of the enteric microbiota influences the fatty acid composition of murine and porcine liver and adipose tissues. Am J Clin Nutr 2009; 89: 1393-401.
119. Hurtado de Catalfo GE, de Alaniz MJ, Marra CA. Influence of commercial dietary oils on lipid composition and testosterone production in interstitial cells isolated from rat testis. Lipids 2009; 44: 345-57.
120. Gromadzka-Ostrowska J. Effects of dietary fat on androgen secretion and metabolism. Reprod Biol 2006; 6 Suppl 2: 13-20.

121. Das UN. Estrogen, statins, and polyunsaturated fatty acids: similarities in their actions and benefits – is there a common link? Nutrition 2002; 18: 178-88.
122. Meeker JD, Godfrey-Bailey L, Hauser R. Relationships between serum hormone levels and semen quality among men from an infertility clinic. J Androl 2007; 28: 397-406.
123. Blaak E. Gender differences in fat metabolism. Curr Opin Clin Nutr Metab Care 2001; 4: 499-502.
124. Williams CM. Lipid metabolism in women. Proc Nutr Soc 2004; 63: 153-60.
125. Childs CE, Romeu-Nadal M, Burdge GC, Calder PC. The polyunsaturated fatty acid composition of hepatic and plasma lipids differ by both sex and dietary fat intake in rats. J Nutr 2010; 140: 245-50.
126. Priego T, Sanchez J, Pico C, Palou A. Sex-differential expression of metabolism-related genes in response to a high-fat diet. Obesity (Silver Spring) 2008; 16: 819-26.
127. Waxman DJ, Holloway MG. Sex differences in the expression of hepatic drug metabolizing enzymes. Mol Pharmacol 2009; 76: 215-28.
128. Lovegrove JA, Gitau R. Personalized nutrition for the prevention of cardiovascular disease: a future perspective. J Hum Nutr Diet 2008; 21: 306-16.
129. Simopoulos AP. The role of fatty acids in gene expression: health implications. Ann Nutr Metab 1996; 40: 303-11.
130. Sampath H, Ntambi JM. Polyunsaturated fatty acid regulation of genes of lipid metabolism. Annu Rev Nutr 2005; 25: 317-40.
131. Calpe-Berdiel L, Escola-Gil JC, Ribas V, Navarro-Sastre A, Garces-Garces J, Blanco-Vaca F. Changes in intestinal and liver global gene expression in response to a phytosterol-enriched diet. Atherosclerosis 2005; 181: 75-85.
132. Moosmann B, Behl C. Secretory peptide hormones are biochemical antioxidants: structure-activity relationship. Mol Pharmacol 2002; 61: 260-8.
133. Brenner RR. Effect of unsaturated acids on membrane structure and enzyme kinetics. Prog Lipid Res 1984; 23: 69-96.
134. Armstrong VT, Brzustowicz MR, Wassall SR, Jenski LJ, Stillwell W. Rapid flip-flop in polyunsaturated (docosahexaenoate) phospholipid membranes. Arch Biochem Biophys 2003; 414: 74-82.
135. Yu BP. Membrane alteration as a basis of aging and the protective effects of calorie restriction. Mech Ageing Dev 2005; 126: 1003-10.
136. Urano S, Sato Y, Otonari T, et al. Aging and oxidative stress in neurodegeneration. Biofactors 1998; 7: 103-12.
137. Fukui K, Omoi NO, Hayasaka T, et al. Cognitive impairment of rats caused by oxidative stress and aging, and its prevention by vitamin E. Ann N Y Acad Sci 2002; 959: 275-84.
138. Li Y, Nara TY, Nakamura MT. Peroxisome proliferator-activated receptor alpha is required for feedback regulation of highly unsaturated fatty acid synthesis. J Lipid Res 2005; 46: 2432-40.
139. Biagi PL, Bordoni A, Hrelia S, Celadon M, Horrobin DF. Gamma-linolenic acid dietary supplementation can reverse the aging influence on rat liver microsome delta 6-desaturase activity. Biochim Biophys Acta 1991; 1083: 187-92.
140. van Dooremalen C, Pel R, Ellers J. Maximized PUFA measurements improve insight in changes in fatty acid composition in response to temperature. Arch Insect Biochem Physiol 2009; 72: 88-104.
141. Harbige LS. Fatty acids, the immune response, and autoimmunity: a question of n-6 essentiality and the balance between n-6 and n-3. Lipids 2003; 38: 323-41.
142. Ergas D, Eilat E, Mendlovic S, Sthoeger ZM. n-3 fatty acids and the immune system in autoimmunity. Isr Med Assoc J 2002; 4: 34-8.
143. Surh YJ. NF-kappa B and Nrf2 as potential chemopreventive targets of some anti-inflammatory and antioxidative phytonutrients with anti-inflammatory and antioxidative activities. Asia Pac J Clin Nutr 2008; 17 Suppl 1: 269-72.
144. Boland LM. Polyunsaturated fatty acid modulation of voltage-gated ion channels. Cell Biochem Biophys 2008; 52: 59-84.
145. Kiecolt-Glaser JK, Belury MA, Porter K, Beversdorf DQ, Lemeshow S, Glaser R. Depressive symptoms, omega-6 : omega-3 fatty acids, and inflammation in older adults. Psychosom Med 2007; 69: 217-24.
146. Tassoni D, Kaur G, Weisinger RS, Sinclair AJ. The role of eicosanoids in the brain. Asia Pac J Clin Nutr 2008; 17 Suppl 1: 220-8.
147. Gerashchenko D, Okano Y, Urade Y, Inoue S, Hayaishi O. Strong rebound of wakefulness follows prostaglandin D2- or adenosine A2a receptor agonist-induced sleep. J Sleep Res 2000; 9: 81-7.
148. Onoe H, Ueno R, Fujita I, Nishino H, Oomura Y, Hayaishi O. Prostaglandin D2, a cerebral sleep-inducing substance in monkeys. Proc Natl Acad Sci U S A 1988; 85: 4082-6.
149. Krueger JM. The role of cytokines in sleep regulation. Curr Pharm Des 2008; 14: 3408-16.
150. Dinan T, Siggins L, Scully P, O'Brien S, Ross P, Stanton C. Investigating the inflammatory phenotype of major depression: focus on cytokines and polyunsaturated fatty acids. J Psychiatr Res 2009; 43: 471-6.
151. Robertson MD, Jackson KG, Fielding BA, Williams CM, Frayn KN. Acute effects of meal fatty acid composition on insulin sensitivity in healthy post-menopausal women. Br J Nutr 2002; 88: 635-40.
152. de Wilde J, Mohren R, van den Berg S, et al. Short-term high fat-feeding results in morphological and metabolic adaptations in the skeletal muscle of C57BL/6J mice. Physiol Genomics 2008; 32: 360-9.
153. Stępień M, Stępień A, Wlazeł RN, Paradowski M, Banach M, Rysz J. Obesity indices and inflammatory markers in obese non-diabetic normo- and hypertensive patients: a comparative pilot study. Lipids Health Dis 2014; 13: 29.
154. Rizzo M, Banach M, Montalto G, Mikhailidis DP. Lipid-lowering therapies and achievement of LDL-cholesterol targets. Arch Med Sci 2012; 8: 598-600.
155. Otocka-Kmiecik A, Mikhailidis DP, Nicholls SJ, Davidson M, Rysz J, Banach M. Dysfunctional HDL: a novel important diagnostic and therapeutic target in cardiovascular disease? Prog Lipid Res 2012; 51: 314-24.
156. Mariscalco G, Sarzi Braga S, Banach M, et al. Preoperative n-3 polyunsaturated fatty acids are associated with a decrease in the incidence of early atrial fibrillation following cardiac surgery. Angiology 2010; 61: 643-50.
157. Cicero AF, Reggi A, Parini A, Borghi C. Application of polyunsaturated fatty acids in internal medicine: beyond the established cardiovascular effects. Arch Med Sci 2012; 8: 784-93.
158. Das UN. Essential fatty acids as possible mediators of the actions of statins. Prostaglandins Leukot Essent Fatty Acids 2001; 65: 37-40.
159. Rizzo M, Nikolic D, Banach M, Montalto G. Statin treatment in the elderly: how much do we know? Arch Med Sci 2013; 9: 585-8.

ANNEX Z:

Simopoulos et al., Ann Nutr Metab 1999;43:127–130.

Meeting Report

Annals of Nutrition & Metabolism

Ann Nutr Metab 1999;43:127–130

Essentiality of and Recommended Dietary Intakes for Omega-6 and Omega-3 Fatty Acids

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The Workshop on the Essentiality of and Recommended Dietary Intakes (RDIs) for Omega-6 and Omega-3 Fatty Acids was held at The Cloisters, National Institutes of Health (NIH) in Bethesda, Md., USA, April 7–9, 1999. The workshop was sponsored by the National Institute on Alcohol Abuse and Alcoholism-NIH, the Office of Dietary Supplements-NIH, The Center for Genetics, Nutrition and Health, and the International Society for the Study of Fatty Acids and Lipids, and cosponsored by several industry groups[1].

The workshop participants consisted of investigators of the role of essential fatty acids in infant nutrition, cardiovascular disease, and mental health. The first two areas were selected because they are the ones where extensive studies involving animal models, clinical intervention trials, and biochemical and physiologic mechanisms and their function have been carried out relative to omega-6 and omega-3 fatty acids. The role of essential fatty acids in mental health is a new, but promising research area.

The workshop was truly international in nature bringing together scientists from academia, government, international organizations, and industry, from Australia, Canada, Denmark, France, Italy, Japan, Norway, Switzerland, United Kingdom, and the United States.

The first two days of the workshop consisted of presentations and extensive discussions. The format of the workshop was Round Table permitting extensive discussion following individual presentations and at the completion of each session. The first day consisted of Session I: Principles to Be Considered in Determining Essentiality and DRIs and Session II: Essential Fatty Acids and Central Nervous System Function. Day two began with Session III: Cardiovascular Disease and ended with Session IV: Relationship of Essential Fatty Acids to Saturated, Monounsatu-

[1] BASF Corp., USA; BASF Health and Nutrition A/S; Bestfoods; ENRECO; F. Hoffmann-La Roche, Ltd.: Groupe Danone; Kraft Foods, Inc.; Martek Biosciences Corporation; Mead Johnson Nutritionals; Ocean Nutrition Canada, Ltd.; Omega Tech, Inc.; Pronova Biocare; and Roche Vitamins, Inc.

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rated, and Trans Fatty Acids. On the morning of the third day, during Session V: Dietary Recommendations and Omega-6:Omega-3 Ratio (LA, LNA, AA, EPA, DHA), industry representatives reported on studies supported by their companies, on clinical interventions, and product development. Representatives from the US Department of Agriculture (USDA), the Pan American Health Organization/World Health Organization (PAHO/WHO) and the Food and Agriculture Organization of the United Nations (FAO) presented their agencies' scientific studies or policies on the dietary intake of fatty acids, especially essential fatty acids, and their activities in the field.

One recommendation deserves explanation here. After much discussion consensus was reached on the importance of reducing the omega-6 polyunsaturated fatty acids (PUFAs) even as the omega-3 PUFAs are increased in the diet of adults and newborns for optimal brain and cardiovascular health and function. This is necessary to reduce adverse effects of excesses of arachidonic acid and its eicosanoid products. Such excesses can occur when too much LA and AA are present in the diet and an adequate supply of dietary omega-3 fatty acids is not available. The adverse effects of too much arachidonic acid and its eicosanoids can be avoided by two interdependent dietary changes. First, the amount of plant oils rich in LA, the parent compound of the omega-6 class, which is converted to AA, needs to be reduced. Second, simultaneously the omega-3 PUFAs need to be increased in the diet. LA can be converted to arachidonic acid and the enzyme, Δ-6 desaturase, necessary to desaturate it, is the same one necessary to desaturate LNA, the parent compound of the omega-3 class; each competes with the other for this desaturase. The presence of LNA in the diet can inhibit the conversion of the large amounts of LA in the diets of Western industrialized countries which contain too much dietary plant oils rich in omega-6 PUFAs (e.g. corn, safflower, and soybean oils). The increase of LNA, together with EPA and DHA, and reduction of vegetable oils with high LA content, are necessary to achieve a healthier diet in these countries.

The afternoon of the third day was devoted to discussion of the omega-6 and omega-3 essential fatty acids and their relationship to other fatty acids. The discussion focussed on specific recommendations for healthy adults, pregnant and lactating women, and the composition of infant formula that will support the growth and development of the formula-fed infant no differently than the breast-fed infant.

Adults

The working group recognized that there are not enough data to determine Dietary Reference Intakes (DRI), but there are good data to make recommendations for Adequate Intakes (AI) for adults as shown in table 1.

Pregnancy and Lactation

For pregnancy and lactation, the recommendations are the same as those for adults with the additional recommendation seen in footnote 1 (table 1), that during pregnancy and lactation women must ensure a DHA intake of 300 mg/d.

Composition of Infant Formula/Diet

It was thought of utmost importance to focus on the composition of the infant formula considering the large number of premature infants around the world, the low number of

Table 1. Adequate Intakes (AI)[1] for adults

Fatty acid	Grams/day (2,000 kcal diet)	% energy
LA	4.44	2.0
(Upper limit)[2]	6.67	3.0
LNA	2.22	1.0
DHA + EPA	0.65	0.3
DHA to be at least[3]	0.22	0.1
EPA to be at least	0.22	0.1
TRANS-FA (upper limit)[4]	2.00	1.0
SAT (upper limit)[5]	–	<8.0
MONOs[6]	–	–

[1] AI = Adequate Intake. If sufficient scientific evidence is not available to calculate an Estimated Average Requirement, a reference intake called an Adequate Intake is used instead of a Recommended Dietary Allowance. The AI is a value based on experimentally derived intake levels or approximations of observed mean nutrient intakes by a group (or groups) of healthy people. The AI for children and adults is expected to meet or exceed the amount needed to maintain a defined nutritional state or criterion of adequacy in essentially all members of a specific healthy population; LA = linoleic acid; LNA = alpha-linolenic acid; DHA = docosahexaenoic acid; EPA = eicosapentaenoic acid; TRANS-FA = trans fatty acids; SAT = saturated fatty acids; MONOs = monounsaturated fatty acids.

[2] Although the recommendation is for AI, the working group felt that there is enough scientific evidence to also state an upper limit (UL) for LA of 6.67 g/d based on a 2,000 kcal diet or of 3.0% of energy.

[3] For pregnant and lactating women, ensure 300 mg/d of DHA.

[4] Except for dairy products, other foods under natural conditions do not contain trans-FA. Therefore, the working group does not recommend trans-FA to be in the food supply as a result of hydrogenation of unsaturated fatty acids or high temperature cooking (reused frying oils).

[5] Saturated fats should not comprise more than 8% of energy.

[6] The working group recommended that the majority of fatty acids are obtained from monounsaturates. The total amount of fat in the diet is determined by the culture and dietary habits of people around the world (total fat ranges from 15–40% of energy) but with special attention to the importance of weight control and reduction of obesity.

women who breastfeed, and the need for proper nutrition of the sick infant. The composition of the infant formula/diet was based on studies that demonstrated support for both the growth and neural development of infants in a manner similar to that of the breastfed infant (table 2).

The following workshop participants have agreed to this summary statement. The copyright of this statement is held by the working group in order to publish it worldwide. The views expressed in this statement do not reflect any official position of the US Department of Health and Human Services.

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Table 2. Adequate Intake (AI)[1] for infant formula/diet

Fatty acid	Percent of fatty acids
LA[2]	10.00
LNA	1.50
AA[3]	0.50
DHA	0.35
EPA[4] (upper limit)	<0.10

[1] AI = Adequate Intake. If sufficient scientific evidence is not available to calculate an Estimated Average Requirement, a reference intake called an Adequate Intake is used instead of a Recommended Dietary Allowance. The AI is a value based on experimentally derived intake levels or approximations of observed mean nutrient intakes by a group (or groups) of healthy people. The AI for children and adults is expected to meet or exceed the amount needed to maintain a defined nutritional state or criterion of adequacy in essentially all members of a specific healthy population; LA = linoleic acid; LNA = alpha-linolenic acid; DHA = docosahexaenoic acid; EPA = eicosapentaenoic acid; TRANS-FA = trans fatty acids; SAT = saturated fatty acids; MONOs = monounsaturated fatty acids.

[2] The working group recognizes that in countries like Japan, the breast milk content of LA is 6–10% of fatty acids and the DHA is higher, about 0.6%. The formula/diet composition described here is patterned on infant formula studies in Western countries.

[3] The working group endorsed the addition of the principal long chain polyunsaturates, AA and DHA, to all infant formulas.

[4] EPA is a natural constituent of breast milk, but in amounts more than 0.1% in infant formula may antagonize AA and interfere with infant growth.

ANNEX AA:

Lands WE. Ann. N.Y. Acad. Sci. 1055:179–192 (2005)

Dietary Fat and Health: The Evidence and the Politics of Prevention

Careful Use of Dietary Fats Can Improve Life and Prevent Disease

WILLIAM E.M. LANDS

ABSTRACT: Every year, more young people start the slow progressive injury that eventually becomes cardiovascular disease and death. It could be prevented with nutrition education, but medical efforts focus more on treatments for older people than on preventing primary causes of disease in young people. Two avoidable risks are prevented by simple dietary interventions: (1) Eat more omega-3 and less omega-6 fats, so tissues have less intense n-6 eicosanoid action, and (2) eat less food per meal to lower vascular postprandial oxidant stress. An empirical diet–tissue relationship was developed and put into an interactive personalized software program to aid informed food choices.

KEYWORDS: essential fatty acids; omega-3; omega-6; polyunsaturated fatty acids (PUFAs); highly unsaturated fatty acids (HUFAs); eicosanoids; thrombosis; inflammation; atherosclerosis; prenylated proteins; platelet activating factor (PAF); oxidized LDL

Much of this chapter echoes talks given 10, 20 and 30 years ago,[1–3] presenting information which failed to percolate effectively into clinical practice or preventive nutrition. As a result, I continue trying to find different methods of effective education so that chronic diseases may be prevented in the elderly. Recent efforts involve two distance-learning web sites with useful "homework" for everyone who wants to learn. One site, for education about essential fatty acids[a] has many details to help people understand the effects of nutritionally essential fatty acids. The other[b] has been hosted by the Office of Dietary Supplements for almost four years, and was upgraded recently with additional background information on how diet affects eicosanoids and how eicosanoids affect health and life.

[a]http://efaeducation.nih.gov/
[b]http://ods.od.nih.gov/eicosanoids/

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The death rate from heart attacks in the United States is among some of the worst in the world.[4] FIGURE 1 demonstrates that death, not life, begins at 40. That is the age at which people begin to lose colleagues and become aware of death. Students feel invulnerable, because not many 30-year-olds die. However, among my peers in their 70s, 1 or 2 per 100 are likely to die of ischemic heart disease in any year.[1] Clinicians say that arterial damage and calcium deposition is just a matter of aging, and that nothing can be done about that. I don't believe that a bit. In Japan, age-specific death rates for coronary heart disease are much lower.[5] However, an apparent inevitability about this is rooted in American lifestyles, all the way back to childhood.

FIGURE 1, presented in 1993,[1] has results added from the PDAY (Pathological Determinants of Atherosclerosis in Youth) study,[6-8] which documented this problem definitively. The problem became apparent 50 years ago, when young soldiers were being killed in Korea. Autopsies showed coronary artery damage in 20-year-old Americans, but not in native Koreans.[9]

Results from the PDAY study[6–8] show that effective primary prevention of atherosclerosis needs to begin with adolescents. FIGURE 1 suggests that by the time American men are 55 years old, most already have inflammatory

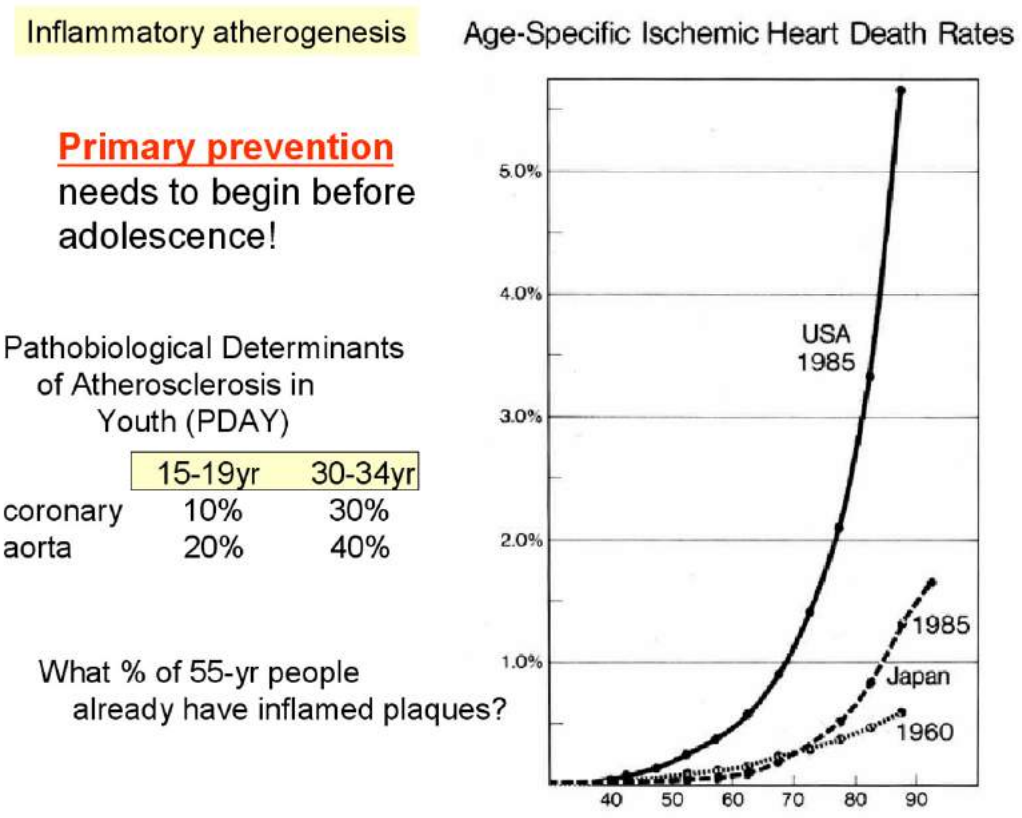

FIGURE 1. Inflammatory atherosclerosis begins developing before adolescence. (Presented in 1993;[1] results added from the PDAY study.[6–8]

plaques in their arteries. Intervention then is really secondary prevention.[10] The effective new technique of electron beam computerized tomography is maturing into a wonderful diagnostic tool.[11] Unfortunately, knowing that you have a lot of calcium in your arteries doesn't tell you how to get rid of it or how to prevent it from accumulating further. We still have a lot of biochemical work to perform.

Real primary prevention doesn't fit programs or goals of pharmaceutical companies, because they cannot make money by preventing the diseases they treat.[10] They work with treatment-oriented groups who aren't interested in educating people about specific dietary interventions that prevent causes of risk. One avoidable risk, an imbalance between intake and expenditure of energy, has received a lot of attention in the last two years. There is a need for further discussion about how it affects vascular inflammation and oxidant stress.

One solution is to eat foods that provide less energy per meal, as noted later in this chapter (FIG. 3). A second avoidable risk is the current severe imbalance between omega-3 and omega-6 nutrients. Most people are completely oblivious to it, but that imbalance is easily corrected by adjusting dietary intakes to more omega-3 and less omega-6 fats. The current imbalance in America is just a happenstance of food marketing.[12] Unfortunately, priorities of corporate health groups will favor the status quo over any action that prevents disease and suffering without adding to corporate profits.[10, 12]

FIGURE 2 shows the consequence of this imbalance. The horizontal axis shows that apparently healthy normal people around the world have different balances of omega 6 and omega 3 in their HUFAs (highly unsaturated fatty acids) because of the different foods they eat.[13,14] The HUFAs are pivotal in the body's healthy self-healing actions. Epidemiology shows that when HUFAs in the body are 70 or 80% omega 6, coronary heart disease rates are around 200 per 100,000.[4] In contrast, people in Spain or Italy have HUFAs containing about 60% omega 6 and 40% omega 3,[10] and their CHD mortality rate is around 120 per 100,000. In Japan, the traditional proportions of HUFAs are about 35–40% omega 6 and 60–65% omega 3, and the heart attack rate in Japan is about one-fourth to one-fifth that in the United States.[5] In Greenland, coronary heart disease is almost undetectable.

Many investigators do not like transnational epidemiology, claiming that genetic diversity impairs interpretation. However, genetic diversity within the United States is probably greater than the mean genetic difference between the United States and Japan. Now we have data from three groups in Quebec, within the same province of the same country on the same continent with the USA. There are urban Quebecois who eat foods that generate HUFA proportions similar to those of people in Chicago and Detroit and New York.[15] On the other hand, in villages north of Quebec City, there are Quebec Cree Indians with different ethnic food habits that give them a different HUFA pattern and mortality rate.[16] Further north in Quebec, Inuits have a lower average n-6

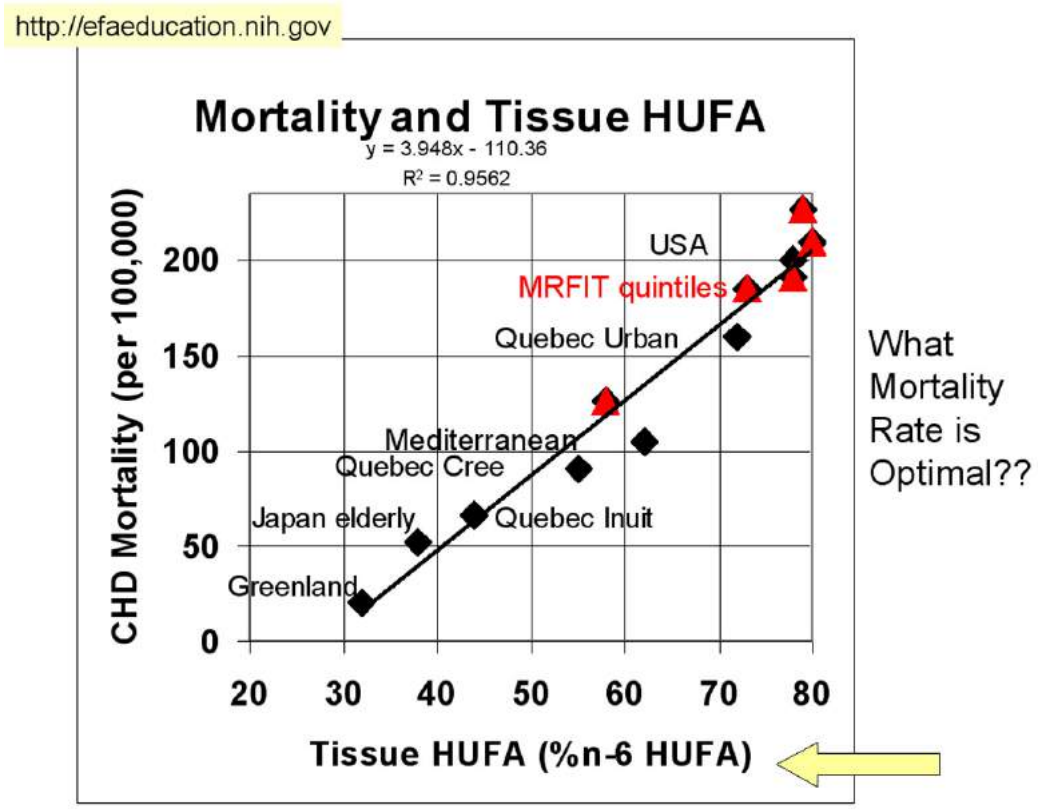

FIGURE 2. Coronary heart disease mortality is proportional to n-6 HUFA in plasma HUFA. Available at <http://efaeducation.nih.gov/sig/personal.html> .

HUFA composition and a lower mortality rate.[17] The trend is clear, even though the Inuit diet has changed tremendously during the last 40 years and is now far more heterogeneous. Indeed, dietary heterogeneity worldwide is the important variable for preventive intervention, more so than genetic variability. Environmental food variability is driving variability in CHD mortality.

Essential fatty acids are polyunsaturated fatty acids (PUFAs) required by all mammals. Like vitamins, these are not produced within the body, and must come from the diet. They are of two types, n-3 and n-6. Linoleic is a n-6 PUFA (18:2n-6) and alpha-linolenic is the n-3 PUFA (18:3n-3). When we eat those acids, our body converts them into longer chain-length, highly unsaturated fatty acids (HUFAs).[c]

What people eat in their diet determines the proportions of HUFAs in their tissue membrane phospholipids. In my first 15 years of academic life, I worked on lipid metabolism[18] and was highly cited on that topic. In 1964, when researchers in Stockholm reported that the n-6 HUFA, arachidonic

[c]http://efaeducation.nih.gov/sig/overviews.html

acid, was converted to the potent hormone, prostaglandin,[19] I hypothesized that HUFA for these hormones comes from the 2 position of the phospholipids in human tissues. But is HUFA converted to eicosanoids on the phospholipids and stored, or is it first hydrolyzed before the free hormone is synthesized? Collaborating with the researchers in Stockholm, I found that the HUFAs in phospholipids were hydrolyzed and then converted to eicosanoids. The hormone then acts at a receptor and generates a signal, which is usually a transient, reversible event that returns to basal state.[20,21]

By the late 1960s, we knew that omega-6 eicosanoids and omega-3 eicosanoids were involved in inflammatory processes. Later, I studied the mechanism by which fatty acid oxygenases act. This requires lipid hydroperoxide activators.[20] Eliminating the peroxides eliminates the ability to make a prostaglandin. Peroxides are also required to activate ribonucleotide reductase, and the free radical is essential to make deoxyribonucleotides for new DNA. The eicosanoids, and the peroxide tone that regulates them, are usually under tight control.[22]

For 15 years I studied aspirin-like non-steroidal anti-inflammatory drugs (NSAIDs),[23,24] working with drug companies to develop new patented drugs for treatment. During the 70s, dozens of eicosanoids were isolated.[21] Nearly all healthy human tissues use eicosanoid modulations of physiologic responses in a rapid transient manner.[20] However, uncontrolled excessive production of omega-6 eicosanoids over prolonged periods of time is associated with heart attacks, thrombotic stroke, arrhythmia, arthritis, asthma, headaches, dysmenorrhea (menstrual cramps), inflammation, tumor metastases and osteoporosis.[21,25] We had been looking at essential vitamin-like fatty acids as "angels" but in excessive amounts they turn into devils. When the body goes out of control, something must be done, and it became my goal to prevent this loss of control.

Two brief narrated presentations covering these general issues are available on the Internet.[d] The distance-learning site for the Office of Dietary Supplements has a section on dietary reference intakes[e] with a graph and citations.[f] These show that most people are eating on the order of 20 times more of the essential vitamin-like n-6 linoleic acid than they need.As with vitamin A and vitamin D, from which the body makes potent hormone-like compounds, there is a probable risk in excessive intakes. The website notes evidence for requiring these substances in amounts on the order of 0.5% of calories or less, but a day's menu in the United States far exceeds that.

To design an effective prevention strategy, one needs to identify causal mechanisms by asking how people die. From this point of view, the role of cholesterol[26, 27] has been portrayed in a misleading fashion for 25 years. Al-

[d]http://efaeducation.nih.gov/sig/beginners.html
[e]http://efaeducation.nih.gov/sig/dietary2.html
[f]http://efaeducation.nih.gov/sig/dri.html

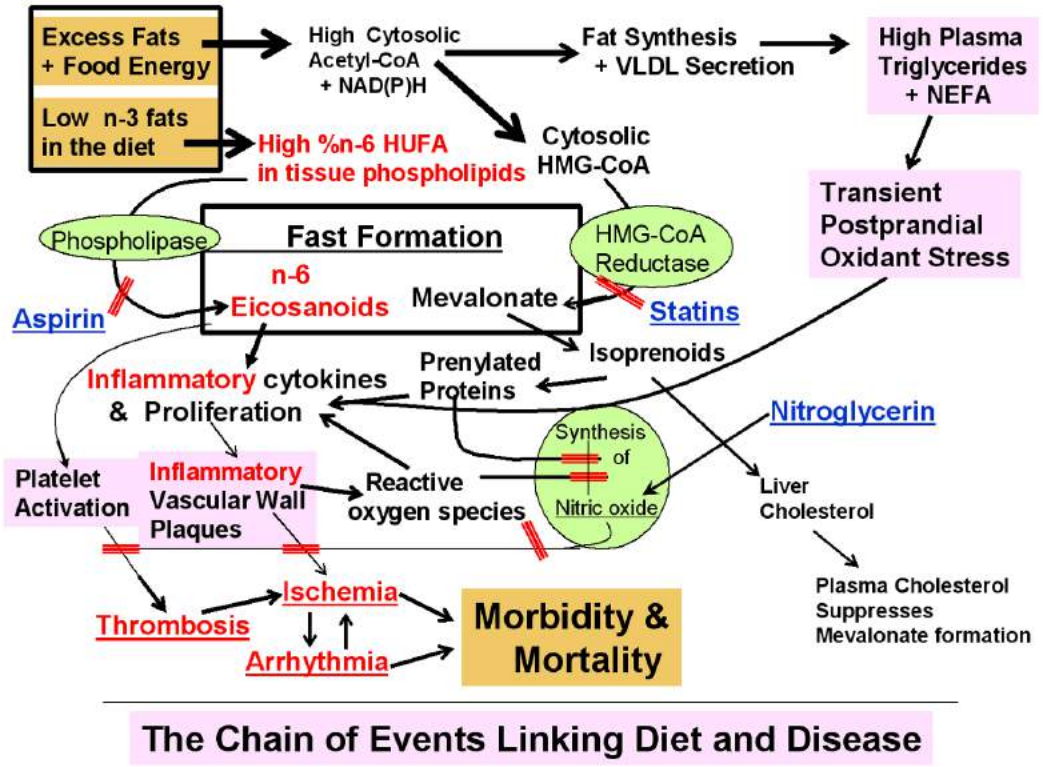

FIGURE 3. Two primary imbalances link diets to disease and death. Modified from an earlier figure[1] at <http://efaeducation.nih.gov/sig/dietdisease.html>.

though some lipoproteins may increase death, cholesterol itself was never proven to kill anyone. However, those who market anti-cholesterol drugs will never mention that fact. To consider primary prevention of heart attacks, we worked backward with the diet–disease concepts shown in FIGURE 3, by stating that a death from heart attack is a death from ischemia, which is exacerbated by arrhythmia, and from thrombosis, which was brought on by a predisposition to inflammatory plaques in the arteries. All three of these processes are exacerbated by n-6 eicosanoids (FIGURE 3). The release of inflammatory cytokines and cell proliferation are enhanced by omega-6 eicosanoids formed from dietary fats.

Inflammatory vascular wall plaques cause ischemia and stimulate thrombosis. Thrombosis is driven by thromboxane, one of the major eicosanoids discovered 29 years ago.[28] Thromboxane causes platelets to clump, causes calcium movement, and causes thrombosis. The omega-6 derivative (TX_{A2}) has the same effect; the omega 3 (TX_{A3}) also has that effect, but to a limited degree.

Aspirin, statins, and nitroglycerin are used widely to diminish the processes set in motion by the two nutritional imbalances shown in the upper left of FIGURE 3. In 1979, when I lectured[2] about these issues in Switzerland and the

Netherlands, the socialized medicine systems in those countries were paying for expensive coronary bypass surgery, and governments were considering preventive nutrition as an economic measure. However, proponents of medications and surgery were not interested in what they regarded as nutritional behavior modification. I scorned the clinicians' disinterest in nutrition at the time, but now I see they may be right. Often it is easier to persuade people to have surgery than to persuade them to change their ideas about what to eat.

What can we do to change people's behavior? Our responsibility is to inform people properly, and their responsibility is to learn what we are trying to teach. The two dietary interventions that people need to learn are shown in the upper left-hand corner of FIGURE 3. Eat more omega-3 and less omega-6 fats to have less-intense n-6 eicosanoid actions. Also, eat less high-energy food per meal to cut transient postprandial oxidant stress three times a day, a thousand times a year. Even when it's 99.9% reversible, the remaining one-tenth of a percent creates another irreversible inflammatory locus every year. By the time people are in their 70s, and the postprandial stress has excess n-6 HUFA and pro-inflammatory eicosanoids, then their condition is seen to move downward in FIGURE 3 and upward in FIGURE 1.

Low-density lipoprotein (LDL) and its phospholipids have some effect on events in FIGURE 3. When inflammatory sites oxidize those phospholipids, they create a platelet activating factor (PAF) agonist that binds the PAF receptor, causing calcium influx plus a stronger inflammatory response. That process has been understood, published, and well accepted for a decade. PAF and PAF mimics are potent calcium ionophores and inflammatory agents in mammalian tissue.[10] Electron beam computerized tomography, described in this volume by Dr. Harvey Hecht,[11] gives a good measure of atherosclerosis by measuring calcium accumulation. We need to learn more about what causes calcium to accumulate and how to prevent it and reverse the effect. Like LDL, high-density lipoprotein (HDL) is an aggregation of proteins, some of which are anti-inflammatory enzymes that destroy PAF and the oxidized phospholipid, preventing them from causing calcium entry and inflammation.[10]

Membrane phospholipids are limited in abundance, and the HUFAs compete for the limited space. If you eat a lot of n-6 fat, it displaces n-3 HUFAs and enhances n-6 eicosanoid formation (FIG. 3). If you eat a lot of n-3 fat, it displaces n-6 HUFAs. The enzymes are promiscuous and don't discriminate much between n-3 and n-6 HUFAs, which means that what you eat can change your body tissue.[13,14]

In the mid-80s, after a Nobel Prize had been awarded for discovery of eicosanoids and their physiology and I had done years of research on lipid metabolism and on NSAID mechanisms, it was well-know that n-6 thromboxane caused heart attacks and n-6 prostaglandins caused inflammation.[25] Pfizer gave me a grant to study the relationship between dietary n-6 and n-3 fats and the proportions of n-6 HUFA in body tissues. I developed and published an empirical predictive equation.[13,29]

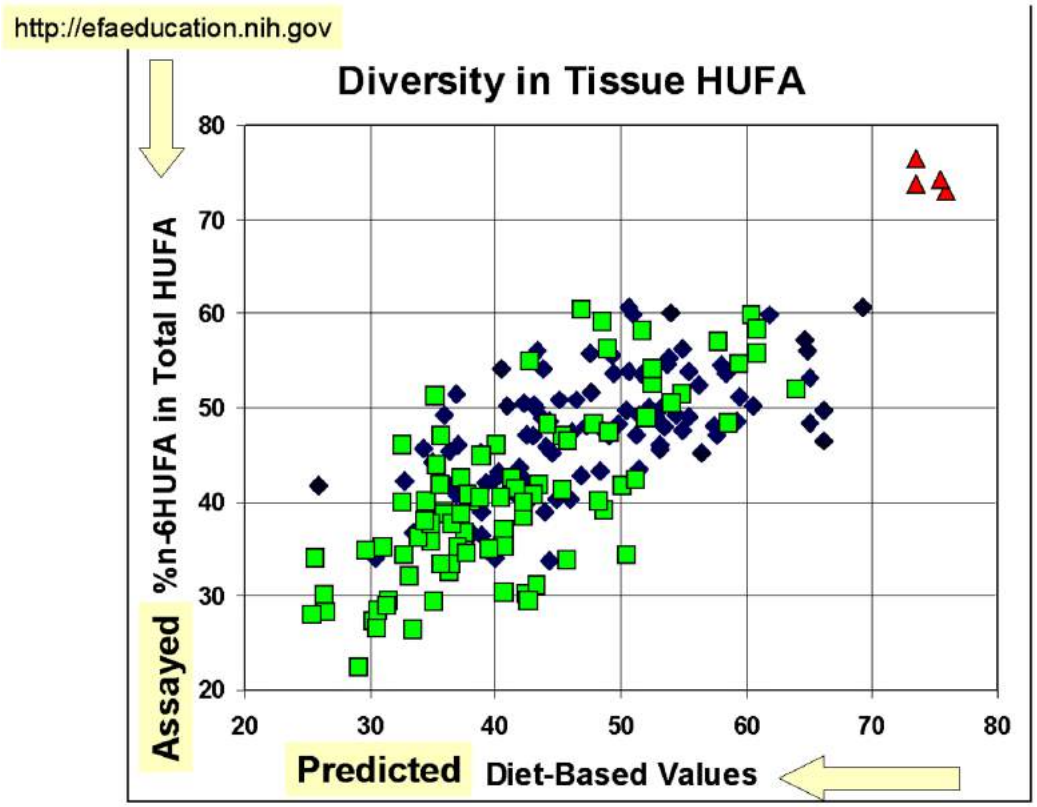

FIGURE 4. Predicted proportions of HUFA fit observed proportions. Previously presented[5] in 2003.

Sadly, I don't think many people read those papers, and I don't think anyone used the equation.[g] I then put it into a spreadsheet so people are not required to do any algebra. They can simply put numbers into a table and let the spreadsheet calculate the likely outcome.[h] FIGURE 4 shows that the equation predicts outcome with a correlation coefficient greater than 0.95. Dietitians carefully monitored the food that people ate, and that information inserted into the equation predicted values of the percentage of n-6 HUFAs in the total HUFA value. There is a good fit between predicted HUFA proportions and those observed by gas chromatographic analysis.[5]

The vertical scatter may be due to proteomics and genomics, whereas horizontal scatter is likely due to imprecise interviews. The group of people represented in the upper right hand in FIGURE 4 were 35-year-old Chicago women. The diamonds represent a group of 45-year-old dietitians in the cities of Japan, and the squares show 55-year-old rural Japanese men. They are all healthy people eating what they choose. The mean value for all people in ei-

[g]http://efaeducation.nih.gov/sig/hufacalc.html
[h]http://efaeducation.nih.gov/sig/dietbalance.html

ther FIGURE 4 or FIGURE 1 would not reveal much about any individual value or the risk of any individual in the group. Those who ate more dietary n-6 as linoleic acid (of which Americans eat a lot) acquired predictably higher proportions of n-6 HUFAs.[13,30]

I used the Pfizer grant to develop a diet–tissue relationship because people doing clinical interventions were making ineffective changes in the diet, too little and too late. Now you can sit down and plan effectively with a little "pocket calculator" at the learning site.[j] The outcome depends on four kinds of dietary essential fatty acid: the 18 carbon n-3 and n-6 and the long-chain n-3 and n-6 HUFA. Diet–tissue calculations can now be handled in a simple spreadsheet, using no algebra or arithmetic.

To illustrate the diet–tissue relationship, the family of curves in FIGURE 5 indicate how different mixtures of n-6 linoleate and n-3 HUFA in daily food create tissue HUFA proportions. Four different ethnic groups are shown as ovals. We still have a long way to go from the HUFA status for average Americans (200 deaths per 100,000 people) to where we might like to be. One cannot choose one's parents or one's genetics, but one can choose the food one puts in one's mouth.[30] It's a simple intervention for someone who is properly informed.

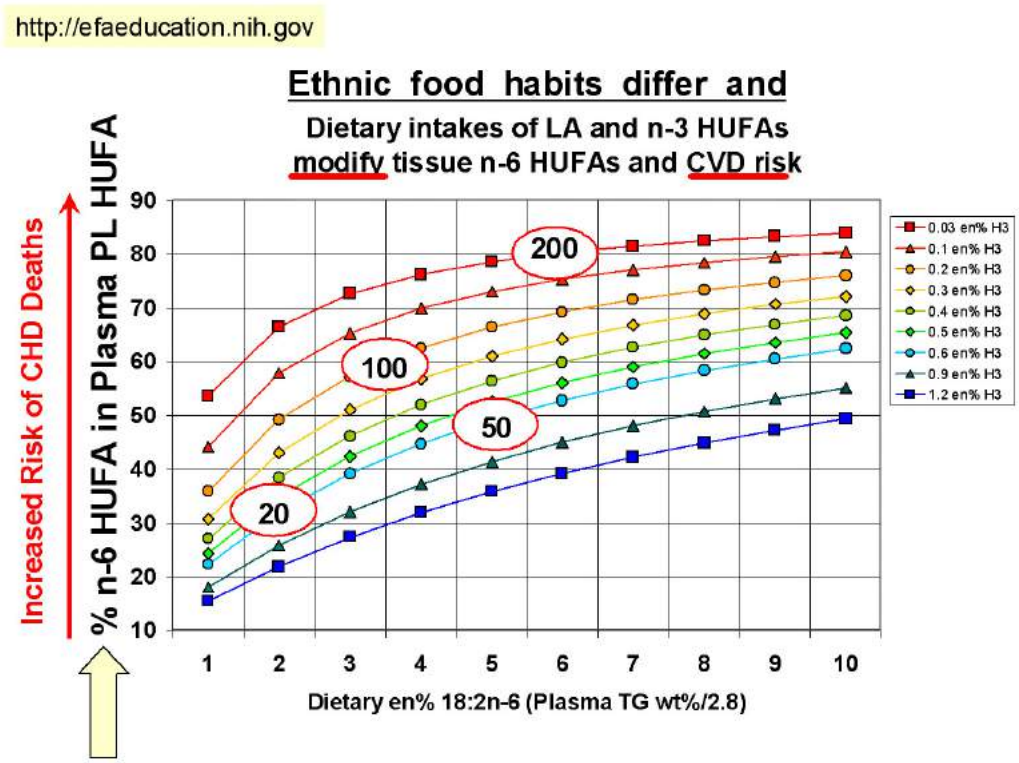

FIGURE 5. Diet–tissue relationship predicts the tissue proportions of n-6 HUFA in tissue HUFA. Available at <http://efaeducation.nih.gov/sig/food2.html>.

[j]http://efaeducation.nih.gov/sig/dietbalance.html

The HUFA proportions for 3,000 Quebec residents ranged from 15 to 91% n-6 HUFA. From FIGURE 2, people can choose their comfort level: what HUFA value they would like to have, and what heart attack risk they would accept. Many people don't want to choose; they want to be told the optimum value. FIGURE 2 makes it obvious that there is no optimum. As you go to higher proportions of n-6 HUFA, the risk grows worse.

Others can see the relationship and risk, but they want to be told which foods are best to eat. Although the distance-learning sites provide a great deal of background information, I decided to use the USDA data base of 6,000 different foods, more than 12,000 servings of food, to create an interactive, computerized, personalized, daily menu-planning program that can be downloaded free.[k] The program allows users to choose foods they want to eat, and it keeps the data managed to let them see whether the daily totals meet their personal goals of cardiovascular risk. The food software takes lifestyle information and tells users what their recommended daily energy allowance is (a value that most sedentary Americans exceed).[31] It also gives some background concepts of risk, and then asks users to choose their risk level and begin choosing foods. Once they look at specific foods, they can begin to see where the omega 6 is entering their diet. For example, the software tells users that the USDA describes a serving of applesauce as having 583 milligrams of 18-carbon omega-6 and only 48 milligrams of omega-3 with no long-chain HUFAs. You can't find any food that doesn't have quite a few milligrams of n-6 linoleate. People producing foods put in n-6-rich oils and raise the level even higher; some breads and muffins have huge amounts. The interactive software shows details and gives the bottom line—total daily total calories and the likely surrogate outcome of HUFA proportions. It also gives a few other dietary facts that dietitians are concerned about and want to convey.

What people really need to know is that their caloric intake is correct and their proportions of eicosanoid precursors are where they want them to be. The nature of a mealtime is that people eat more than they need at that moment and then have transient excess. That excess and its transient postprandial oxidant stress is the beginning of a problem.

If people ate only one meal a day, they would have a large bolus of carbons and electrons entering metabolic pathways. The liver would to make free radicals (and also make cholesterol) and the endothelial cells would respond with oxidant stress due to that postprandial bolus. If people ate smaller meals, five times a day, they would have smaller and more reversible oxidant stress; it would be still lower, with more n-3 and less n-6 HUFAs in the tissues. To take in less energy per meal, people should eat several small meals or snacks if they want. One of the underlying rules is to eat no more than you need.

The top predicted causes of death and disability[32] worldwide for 2020 (ischemic heart disease and unipolar major depression), and three top causes

[k]http://efaeducation.nih.gov/sig/kim.html

in developed regions (ischemic heart disease, cerebrovascular disease, and unipolar major depression) all seem linked to imbalanced omega-3 and omega-6 actions in tissues. We knew about n-6 eicosanoid mechanisms for thrombosis and inflammation 25 to 30 years ago. In the past five years, increasing evidence suggests that major depression, post-partum depression, and behavior disorders also relate to imbalances in omega-3 and omega-6 dietary intakes. Additional evidence showed important actions of n-3 HUFAs in brain function,[33] and the American Heart Association recently urged putting more n-3 HUFAs into daily diets.[34] The growing awareness of the importance of balancing n-3 and n-6 fats is evident from the single major personal health change recommended recently by the health and nutrition division members of the American Oil Chemists' Society: to eat more fish and take an omega-3 supplement.[35] Also, their most frequent advice to other people was to eat more seafood and fish.

In this volume, Dr. Richard Cutler[36] has given us a philosophical view of these issues. We tend to simplify matters that are complex. We use words like "gene" or "the genome" or "inflammation" or "aging," as if these phenomena were a single entity when, in fact, they are a mass of ill-defined parts. On the other hand, some things that are actually simple seem complex. FIGURE 3 outlines the chain of events that lead from food choices to morbidity and mortality. Three types of medication (aspirin, nitroglycerin, and statins) are noted, to show the step in the process at which these familiar drugs intervene. However, when we recognize the initial imbalances in our nutrition that cause cardiovascular death, we can design more effective primary prevention and better nutrition education for the public.

Inflammation was always important in vascular disease, and it was driven by excessive n-6 eicosanoid actions amplifying results of excessive food energy, producing more carbon and electrons than the body could deal with at any given moment. That led to increased cytosolic acetyl-CoA and HMG-CoA, which led to more mevalonate and prenylated proteins (FIG. 3) which are having effects that we didn't recognize 20 years ago. Some prenylated proteins block synthesis of nitric oxide and enhance inflammation. They come about because HMG-CoA reductase is pushed into making more mevalonate than necessary. We knew 25 years ago that plasma cholesterol gave negative feedback that suppressed cholesterol biosynthesis. We subsequently learned that plasma cholesterol suppresses the proteolysis of sterol regulatory element-binding protein, slowing activation of genes expressing fat-forming enzymes. The misimpression that cholesterol (a marker of excessive HMG-CoA reductase action) has been killing people, when the killers are actually vascular inflammation, thrombosis and arrhythmia, is one of the tragedies of biomedical science.[26,27]

The discussion in FIGURE 3 notes that lipoprotein (LDL) has phospholipids that form highly potent inflammatory agents on oxidation, regardless of cholesterol. Phospholipids in the LDL may be deadly. HDL may have cholesterol

(and it has phospholipids), but it has enzymes that neutralize inflammatory oxidized phospholipid PAF mimics and PAF.[37] So HDL is beneficial and LDL is harmful, but it's absurd to talk about "bad cholesterol" and "good cholesterol." We can hope that the tragic detour that delayed understanding of nutritional causes and preventive interventions is nearly over, and that the organizations that could provide the necessary information will do so. Then a new day will dawn for the young people in whom every successive year perpetuates the slow progressive injury that leads to cardiovascular disease and death.

REFERENCES

1. LANDS, W.E.M. 1993. Eicosanoids and health. Ann. N.Y. Acad. Sci. **676**: 46–59.
2. LANDS, W.E.M., B. PITT & B.R. CULP. 1980. Recent concepts on platelet function and dietary lipids in coronary thrombosis, vasospasm and angina. Herz **5:** 34–41.
3. LANDS, W.E.M., P.R LETELLIER, L.H. ROME, *et al*. 1973. Inhibition of prostaglandin biosynthesis. Adv. Biosci. **9:** 15–27.
4. LANDS, W.E.M. 2003. Diets could prevent many diseases. Lipids **18**: 317–321.
5. LANDS, W.E.M. 2003. Functional foods in primary prevention or nutraceuticals in secondary prevention? Curr. Top. Nutraceutical Res. **1:** 113–120.
6. PDAY RESEARCH GROUP. 1990. Relationship of atherosclerosis in young men to serum lipoprotein cholesterol concentrations and smoking. A preliminary report from the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. JAMA **264:** 3018–3024.
7. MCGILL, H.C., JR., C.A. MCMAHAN, A.W. ZIESKE, *et al*. 2000. Associations of coronary heart disease risk factors with the intermediate lesion of atherosclerosis in youth. The Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. Arterioscler. Thromb. Vasc. Biol. **20:** 1998–2004.
8. ZIESKE, A.W., G.T. MALCOLM & J.P. STRONG. 2002. Natural history and risk factors of atherosclerosis in children and youth: the PDAY study. Pediatr. Pathol. Mol. Med. **21:** 213–237.
9. ENOS, W.F., R.H. HOLMES & J. BEYER. 1953. Coronary disease among United States soldiers killed in action in Korea. JAMA **152**: 1090–1093.
10. LANDS, W.E.M. 2003. Primary prevention in cardiovascular disease: Moving out of the shadows of the truth about death. Nutrition, Metabolism and Cardiovascular Diseases **13**: 154–164.
11. HECHT, H.S. 2004. Cardiovascular risk assessment. Ann. N.Y. Acad. Sci. **1055:**this volume.
12. NESTLE, M. 2002. Food Politics: How the Food Industry Influences Nutrition and Health. University of California Press, Berkeley, CA.
13. LANDS, W.E.M., B. LIBELT, A. MORRIS, *et al*. 1992. Maintenance of lower proportions of n-6 eicosanoid precursors in phospholipids of human plasma in response to added dietary n-3 fatty acids. Biochem. Biophys. Acta **1180:** 147–162.

14. LANDS, W.E.M. 1995. Long-term fat intake and biomarkers. Am. J. Clin. Nutr. **61**(Suppl)**:** 721S–725S.
15. DEWAILLY, E., C. BLANCHET, S. GINGRAS, *et al*. 2001. Relations between n-3 fatty acid status and cardiovascular disease risk factors among Quebecers. Am. J. Clin. Nutr. **74:** 603–611.
16. DEWAILLY, E., C. BLANCHET, S. GINGRAS, *et al.* 2002. Cardiovascular disease risk factors and n-3 fatty acid status in the adult population of James Bay Cree. Am. J. Clin. Nutr. **76:** 85–92.
17. DEWAILLY, E., C. BLANCHET, S. LEMIEUX, *et al*. 2001. n-3 Fatty acids and cardiovascular disease risk factors among the Inuit of Nunavik. Am. J. Clin. Nutr. **74**: 464–473.
18. LANDS, W.E.M. 1965. Lipid metabolism. Ann. Rev. Biochem. **34:** 313–346.
19. BERGSTROEM, S, H. DANIELSSON, D. KLENBERG *et al*. 1964. The enzymatic conversion of essential fatty acids into prostaglandins. J. Biol. Chem. **239:** PC4006–4008.
20. LANDS, W.E.M. 1979. The biosynthesis and metabolism of prostaglandins. Ann. Rev. Physiol. **41:** 633–652.
21. SAMUELSSON, B. 1979. Prostaglandins, thromboxanes, and leukotrienes: formation and biological roles. Harvey Lect. **75:** 1–40.
22. KULMACZ, R.J. & W.E.M. LANDS. 1997. Peroxide tone in eicosanoid signaling. *In* Oxidative Stress and Signal Transduction. H.J. Forman & E. Cadenas, Eds.: 134–156. Chapman & Hall. New York.
23. ROME, L.H. & W.E.M. LANDS. 1975. Structural requirements for time-dependent inhibition of prostaglandin biosynthesis by anti-inflammatory drugs. Proc. Natl. Acad. Sci. USA **72:** 4863–4865.
24. HANEL, A.M. & W.E.M. LANDS. 1982. Modification of antiinflammatory drug effectiveness by ambient lipid peroxides. Biochem. Pharmacol. **31:** 3307–3311.
25. LANDS, W.E.M. 1986. Fish and Human Health, Academic Press. Orlando, FL.
26. MOORE, T.J. 1989. Heart Failure. Simon & Schuster. New York.
27. RAVNSKOV, U. 2000. The Cholesterol Myths. New Trends Publishing, Inc. Washington, DC.
28. HAMBERG, M., J. SVENSSON & B. SAMUELSSON. 1975. Thromboxanes: a new group of biologically active compounds derived from prostaglandin endoperoxides. Proc. Natl. Acad. Sci. USA **72:** 2994–2998.
29. LANDS, W.E.M., A.J. MORRIS & B. LIBELT. 1990. Quantitative effects of dietary polyunsaturated fats on the composition of fatty acids in rat tissues. Lipids **25:** 505–516.
30. LANDS, W.E.M. 1991. Biosynthesis of prostaglandins. Annu. Rev. Nutrition **11:** 41–60.
31. Recommended Dietary Allowances, 10th Edition. 1989. National Academy Press, Washington, DC.
32. MURRAY, C.J.L. & A.D. LOPEZ. 1997. Alternative projections of mortality and disability by cause 1990–2020: global burden of disease study. Lancet **349:** 1498–1504.
33. SALEM, N., JR., B. LITMAN, H.Y. KIM *et al*. 2001. Mechanisms of action of docosahexaenoic acid in the nervous system. Lipids **36:** 945–959.
34. KRIS-ETHERTON, P.M., W.S. HARRIS & L.J. APPEL. 2002. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. Circulation **106:** 2747–2757.

35. What the experts eat: the Health & Nutrition Division weighs in with nutrition advice. 2003. Inform (American Oil Chemists' Society) **14:** 116-117.
36. CUTLER, R.G. 2005. Oxidative stress profiling. Part 1. Its potential importance in the optimization of human health. Ann. NY Acad. Sci. **1055:** 93–135.
37. MARATHE, G.K., G.A. ZIMMERMAN & T.M. MCINTYRE. 2003. Platelet-activating factor acetylhydrolase, and not paraoxonase-1, is the oxidized phospholipid hydrolase of high density lipoprotein particles. J. Biol. Chem. **278:** 3937–3947.

ANNEX AB:

The World's Healthiest Foods (WHFoods.com) The George Mateljan Foundation (non-profit) "*A New Way of Looking at Proteins, Fats and Carbohydrates*" published January 2007.
http://web.archive.org/web/20070104020351/http:/whfoods.com/genpage.php?tname=faq&dbid=7#polyun

Eating Healthy

- WHFoods List
- Important Q&As
- Essential Nutrients
- Food Advisor
- All About Organic Foods
- Ask George Your Questions

Cooking Healthy

- WHFoods Kitchen
- Seasonal Eating
- Over 100 Recipes
- In Home Cooking Demo

Feeling Great

- Feeling Great Menu
- Healthy Way of Eating
- How Foods Help You Stay Healthy
- For the Entire Family
- Eating Right for Your Disease
- 5 Health-Promoting Diets
- Meal Planning for Health Conditions

Community

- Who We Are
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A New Way of Looking at Proteins, Fats and Carbohydrates

Topics

Discussion

Introduction

Most traditional discussions of macronutrients - carbohydrates, fats, proteins - revolve around the issue of quantity, either as the gram amount of these molecules necessary per day, or as the percentage of the diet that they should each contribute. While this is an important issue to consider, when it comes to these essential nutrients, quantity should not be the only concern. These three classes of macronutrients are complex groups, each of which contains a variety of components. You can eat the same quantity of protein, carbohydrate and fat, but deliver very different nutriture to your body depending on the sources of these molecules. For example, both lard and olive oil are fats, but the information they provide to your cells is very different. Therefore, it is not just quantity, but quality that matters.

Following is an overview of macronutrients that will explore this topic, so you can get a clear picture of how the macronutrients in the World's Healthiest Foods promote health and wellness.

A New Way of Looking at Carbohydrates

Carbohydrates are a varied combination of both very small and very large molecules that comprise about 40 to 45 percent of the energy supply for your body. In addition, certain types of carbohydrates, such as fiber and resistant starches don't get taken into your body for energy, but play important health-promoting roles in your gastrointestinal tract, supporting digestion and absorption, and helping you eliminate toxins and waste products.

Carbohydrates are are composed of carbon, hydrogen, and oxygen, which are arranged into small units called sugars, or monosaccharides. Small carbohydrates, like glucose or sucrose (table sugar) are composed of one or two sugar units, respectively, and are the molecules that give food a sweet taste. These molecules are sometimes called "simple sugars" because they are small (only one or two units), and are quickly digested, providing immediate energy to the body.

Larger carbohydrate molecules, which include fibers and starches, are composed of at least 10 monosaccharides linked together. These large carbohydrates, called polysaccharides (poly=many) may contain up to several hundred monosaccharides linked together in different ways. Another term commonly used to describe carbohydrates is *oligosaccharides*, a type of carbohydrate molecule that is in-between polysaccharides and monosaccharides in size, and features two to ten monosaccharides bonded together.

Let's look at each of these types of carbohydrates and how the food you eat influences the quality of these important nutrients you receive.

The Simple Sugars: Monosaccharides and Disaccharides

Monosaccharides

Monosaccharides are true simple sugars since, as one sugar unit only, they exist in the form in which they can be directly absorbed into your body upon ingestion. Unlike the other carbohydrates, they don't require being broken down during digestion, so when you eat a food containing monosaccharides, these sugars quickly get into your bloodstream, increasing your blood sugar and providing immediate energy. Examples of monosaccharides include glucose, fructose and galactose.

Monosaccharides are present in most foods in at least some amount, but are particularly high in foods such as ripe fruit, and honey. Monosaccharides are an important energy source, but when too much of these simple sugars are consumed at once--especially when they are not balanced by complex carbohydrates like oligosaccharides or polysaccharides that take longer to digest and thus help maintain longer-term energy production--monosaccharides can cause a large increase in blood sugar, followed by an abrupt drop. The result is a jolt of energy quickly followed by a feeling of being tired, shaky, or run-down soon afterward. This type of fluctuation in blood sugar, if it occurs frequently, can lead to blood sugar dysregulation conditions such as hypoglycemia and diabetes mellitus. Proceesed foods often add high amounts of monosaccharides such as fructose and glucose to promote a sweet taste, which sells more product, but does not sustain health.

Disaccharides

Disaccharides contain two monosaccharides (di=two) bonded together, and include sugars such as lactose (milk sugar), sucrose (table sugar), maltose and isomaltose (sugars formed from the breakdown of starch). Disaccharides are similar to monosaccharides; that is, they provide sweet taste to food and quick energy, which is why they are considered "simple sugars" as well. As such, disaccharides also are highly represented in processed foods, and their frequent consumption can lead to blood-sugar disregulation, the same as monosaccharides.

Since these carbohydrates contain two sugars, disaccharides require some digestion to break them into two one-sugar units for absorption, and since each disaccharide is unique, each has its own digestive enzyme. For example, the enzyme *sucrase* can cut sucrose into its two individual sugar units; *lactase* cuts lactose into its two sugars. For most disaccharides, these enzymes area readily secreted into the intestines after consuming a meal, and digestion of the disacchrides proceeds rapidly. The exception appears to be with lactose (milk sugar).

Many people lack the enzyme *lactase* and are therefore unable to breakdown lactose, a condition called lactose intolerance, which makes the consumption of dairy products problematic for many people. Lactose intolerance, which occurs more

frequently as we age, is quite common in adults. In lactose intolerance, the undigested lactose is not absorbed and can promote growth of unfriendly bacteria in the upper intestinal tract, a condition called small bowel overgrowth. These bacteria ferment the lactose, producing gas in the small intestine that causes great discomfort, along with acid, which can cause heartburn and nausea. Even more problematic, the acid produced by this bacterial fermentation can degrade the lining of the small intestine, injuring the intestinal tract cells. This damage compromises the ability of the intestinal cells to produce enzymes for digestion, so even less disaccharide digesting enzymes are produced, and a cycle of maldigestion is perpetuated. Diets that limit disaccharides may be of benefit for persons with these concerns, and a person with lactose intolerance should not consume lactose-containing foods without having a source of lactase either in the food or taken with the food. Some studies suggest that Lactobacillus supplements are beneficial in this respect as well.

The Polysaccharides: Starch, Fiber and Resistant Starch Starch

Plants store their energy by stringing together many glucose units into a long complex of several hundred to several thousand sugar (glucose) molecules. Plant foods that contain stored energy, for example seeds that must provide energy for the young plant when it starts growing, are high in starch. When the young plant starts growing, the starch is broken down into glucose for energy.

Starch

When you eat foods that contain starch, like corn or potatoes, your body uses this starch in much the same way. Since your body must breakdown this very large molecule to individual sugar units before they can be digested, the digestion of starch takes longer than that of disaccharides; therefore, starch provides an extended, or sustained source of energy. Because they do not lead to immediate bloodsugar spikes followed by a low, but instead a more moderate, longer-term elevation of blood sugar, starches are thought to be better for health and energy.

Starches are called complex carbohydrates because they are so large. Two main types of starches exist in food: amylose and amylopectin. These starches differ in how the individual sugars they contain are linked together. This difference results in differences in how easy it is for your body to cut the starches into their individual sugar units. Amylopectin is more quickly digested than is amylose; therefore, foods that contain higer amylose than amylopectin are often suggested as substitutions for people with bloodsugar control problems, like diabetes.

Starch digestion is also influenced by how the starch is packed in the food. When food is whole, or in its natural state, marcromolecules are folded together, and starch can be encased in protein or fiber or other large molecules that must be digested before the starch itself becomes available for digestion. The result of this packaging, again, is to slow down the absorption of the individual sugar units from the starch, and to provide extended, sustained energy for a longer-term, moderate rise in blood sugar after a meal. In contrast, processed foods have removed this complex interaction. In processing, the macromolecules are initially pulled apart from each other, then added back separately. The result is starch that is more accessible for quick digestion and absorption, and causes quicker, higher rises in blood sugar, looking more like a disaccharide than a starch. Therefore, people with blood sugar control concerns, such as hypoglycemia, insulin resistance or diabetes can benefit from eating whole foods and avoiding high-starch, processed foods.

Fiber

Dietary fibers are also polysaccharides and are, therefore, considered complex carbohydrates; however, the sugar units in fiber are linked (bonded) together in such a way that your body can't break the bonds and digest them. Instead, fibers transit through your small intestines and make it all the way to your large intestine intact. This ability to move through your system to your large intestine helps speed the transit times of wastes excreted from your body; for this reason, fiber helps to support your health by reducing constipation and promoting the excretion of toxins and wastes.

Fibers that promote overall healthy digestion and waste excretion are found in vegetables, grains, and legumes and are well represented in whole foods. Often, when processed, foods have these fibers removed. For example, bran contains high levels of fibers and is removed when grains are processed. Fruit skins are also high in fiber, but are often removed when the fruit is

processed for a fruit-containing product.

Much has been written about the health-promoting benefits of fiber, and ample numbers of studies support an association between high-fiber diets and a decrease in risk of many types of cancers, including colon cancer and breast cancer. Some of this benefit comes from the ability of fiber to bind and remove toxins, and to promote healthy digestion. Recent research suggests, however, that fiber provides its health-protecting benefits in other ways as well, and one of the most important appears to be its ability to promote healthy intestinal tract bacteria.

Your large intestine contains a multitude of beneficial bacteria that are required for your body's health. They are called the "friendly flora," or the beneficial symbiotic microbes, and they support the health of your whole body by promoting healthy immune function and providing important molecules to your intestinal tract cells to promote their growth, thus sustaining overall intestinal tract integrity. These microbes use some of the fibers you eat as fuel for their own growth, and through their own metabolism produce molecules called short-chain fatty acids (SCFA). SCFA production by these friendly flora has been associated with a decrease in cancerous colonic cells, reduction of serum cholesterol, and maintenance of healthy blood sugar levels and healthy intestinal tract cell walls.

Not all fiber is fermented by the friendly flora in your intestinal tract. Some, as discussed above, goes through your entire system unchanged, binding toxins and waste products as it goes, and promoting healthy elimination. Some fibers can be fermented by microbes of all types, while other fibers are preferentially fermented by the "friendly flora," the bacteria that are most beneficial to your body, including Bifidobacteria and Lactobacillus. When these friendly bacteria are given their favorite types of fibers, called "prebiotic fibers," they will flourish, significantly improving the health of your digestive tract. Excellent sources of these prebiotic fibers include foods such as Jerusalem artichoke, chicory, rice fiber, and soy fiber.

The classical way of talking about fiber to divide it into two types, soluble or insoluble fiber, a classification determined by how much water a type of fiber holds. New research, however, suggests that fiber has a multitude of activities besides holding water, and that this classical distinction is not adequate. Providing a full range of all types of fibers, including prebiotic fibers, will support your immune system, and enhance healthy digestion, absorption, and the removal of wastes and toxins. In fact, the health of your gastrointestinal tract is dependent upon your consumption of the variety of fibers well-represented in the World's Healthiest Foods.

Resistant Starch

A final category of polysaccharides, or complex carbohydrates, is that of resistant starch. Resistant starch gets its name because, although it is starch, it is resistant to digestion in the small intestine. The result of this resistance is that this type of starch acts more like fiber than starch, and travels through the intestinal tract until it reaches the large intestine where, like fiber, is may be fermented by the bacteria in the colon. Research has shown that resistant starch promotes the generation of SCFAs by the bacteria in the large intestine, and therefore has many of the same health-promoting abilities as fiber. Resistant starch is found in whole grains such as brown rice, barley, whole wheat, and buckwheat.

A New Way of Looking at Protein

Proteins are extremely important because they constitute the majority of the structural tissue in your body, such as bone and the connective tissues that provide the shape and form to which your cells attach. The eminent importance of protein to our life is reflected in the term itself: protein is derived from the Greek term *protos*, which means "taking first place." Proteins are involved in just about every function in your body, in particular, enzymes are proteins, and enzymes are the molecules in the body that do much of the work like building new tissue, breaking down old tissue, and even providing channels in your cells' membranes to let in necessary nutrients, plus removing wastes and toxins from the body by metabolizing, or breaking them down.

Your body is constantly making new proteins to replenish those lost from tissue damage, to fight invaders and protect your body, and to provide for growth. For example, the antibodies of your immune system, some hormones of your endocrine system, the enzymes in your digestive system, and the blood coagulating factors of your circulatory system are all made of proteins.

Amino Acids

Proteins are made up of smaller molecules called amino acids that are strung together by chemical bonds like beads on a chain. To become an active, functional protein, this string of amino acids folds in on itself forming a twisted and entwined, three-dimensional structure. Proteins come in many sizes. Some chains of amino acids are quite small, for example, the hormone insulin, a protein which is only 51 amino acids long. Most proteins, however, are larger. Most of proteins in your body contain between 200-400 amino acids, for example, many of the enzymes your body uses for digestion of food such as chymotrypsin, which is 245 amino acids, or pepsinogen, which is 362 amino acids. Some of the proteins in your body are very large. The protein hemoglobin, which carries oxygen in your blood to your cells, is made of 574 amino acids; the immunoglobulins that help protect your body from infectious invaders contain 1,320 amino acids, and the ATPase complex, the enzyme at the end of the electron transport chain in the mitochondria (the energy-production factories in our cells), is composed of 9 large protein chains containing around 3,000 amino acids in total.

Individual proteins also can join together to form large protein complexes. The largest protein complexes in your body are the proteins that make up the matrix of your bone, skin, nails, hair, tissue and teeth upon which all your cells attach. These include proteins like collagen, elastin (which gives your skin its elasticity), and keratin. Collagen, for example, is composed of three strings of 1,000 amino acids each that twist together into a long, cylindrical chain of 3000 amino acids. This chain then complexes with many other collagen chains to form a thicker, stronger cylinder, called a fibril. Fibrils can have 6 to 20 or more collagen chains per section, which means they can contain tens of thousands of amino acids in one protein structure. Fibrils provide the structure upon which your bone mineralizes, and they crisscross throughout your soft tissue to keep your cells in contact with each other.

The single amino acid is similar to a simple sugar, in that it is the single unit your body works with to build larger protein chains. And, in a manner similar to the digestion of carbohydrates, your body breaks proteins down to amino acids during the digestion process, taking in only the small single amino acid unit, or sometimes a two or three amino acid unit. Like carbohydrates, amino acids are composed of carbon, hydrogen, and oxygen, but unlike carbohydrates, amino acids also contain nitrogen. In fact, amino acids are your body's way of getting this necessary component: nitrogen.

How Much Protein Do I Need and How Do I Get It?

A healthy adult is estimated to need around 40 to 65 grams of amino acids per day. If this is not provided in the food you eat, your body will begin to break down its own muscle to support its need for amino acids. Inadequate intake of amino acids from protein can lead to stunting, poor muscle formation, thin and fragile hair, skin lesions, a poorly funcitoning immune system, and many other symptoms. You get these amino acids primarily from the protein in plant and animal foods, which requires digestion. Free amino acids, which require no digestion, just absorption in the small intestines, are also present in whole foods, but are often removed during processing. Although vegetables and grains do provide some proteins, you get the majority of your protein from nuts, legumes, eggs, fish, meats and dairy products.

In processed foods, protein is sometimes provided as hydrolyzed proteins, which means it has been chemically cut into smaller chains of from two to 200 amino acids, which are called peptides. Some specially produced foods for hospital or healthcare use are made of elemental amino acids; these products provide the free amino acids themselves and require no digestion before absorption.

Peptides are short strings of amino acids bonded together. Since there are twenty different amino acids, a great number of different peptides can be created. When peptides link together, they undergo chemical processes that cause their molecules to fold in upon themselves, creating a complex structure classified as a protein.

The Essential Amino Acids: What Are They and Why Do I Need Them?

Amino acids are made into approximately 20 different versions, and proteins require all of these at some level, so for your body to make a protein, it must have all 20 amino acids available. Your body can synthesize many of these amino acids from other molecules; however, nine amino acids cannot be made in your body. These are called the "essential" amino acids, because your diet must supply them for your survival. Examples of essential amino acids include leucine, methionine,

phenylalanine, and tryptophan.

All proteins have these essential amino acids, but your body requires them in certain amounts and ratios to each other. Animal foods contain these amino acids in ratios that are similar to those found in humans, while most plant-based foods do not. In the past, people were concerned that vegetarians and people whose diets consisted mostly of plant foods were at risk of protein deficiency since they were not eating "complete" proteins. More recently, this old theory has been rejected. Researchers and healthcare practitioners have suggested that since different plant-based foods provide different essential amino acids, eating a varied diet featuring whole grains, legumes, and vegetables does provide all of these important building blocks to sustain health and promote vitality. In addition, some plant-based foods, such as soy, actually feature an essential amino acid protein profile similar to animal-based foods.

A New Way of Looking at Fats

What are Fats?

Fats are probably the most complex of the macromolecules in foods because there are so many different types of fats. Unfortunately, fats have been given a bad reputation, in part because fat is the way we store excess calories, and in part because saturated fats, trans-fatty acids, and cholesterol have been asociated with health conditions like cardiovascular disease and obesity. The facts are, however, that not only are all fats not bad, but some fats have been shown to be health-promoting, and some fats are absolutely essential for your health. So, when you think about fats, the quality of the fat, and therefore the quality of the food from which you are getting the fat, really matters.

Fats, which are also referred to as *lipids*, are composed of carbon, hydrogen, and oxygen like the other macromolecules, but fats are designed in a structure that makes them insoluble in water. We call this *hydrophobic* (hydro=water; phobic=hating). Fats are chemically described as either unsaturated, monounsaturated or polyunsaturated. The saturated fats are straight molecules that form solids at room temperature, such as butter and the fats found in meat. Monounsaturated fats, like olive oil, are liquids at room temperature but form solids in the refrigerator. Polyunsaturated fats, which are found in high amounts in oils from grains and seeds, such as flaxseed oil, are liquid at room temperature and remain liquid even when cooled.

This different physical property of fats is one reason your body uses so many different types. One extremely important role of fats is as a major component of all the membranes in your cells. You cell membranes contain all of these different kinds of fats -- unsaturated, monounsaturated, and polyunsaturated -- however, they are needed in different amounts. Your cells primarily need polyunsaturated fats along with some monounsaturated fat to keep your membranes, and therefore your cells, flexible and moveable. When levels of saturated fat are too high, cell membranes become inflexible and don't function well, so they can't protect the internal parts of the cell, such as its DNA, as well.

Saturated Fats and the Controversy of the "Bad" Fat

More than 50 years ago, data linking consumption of saturated fats to elevated blood cholesterol levels, atherosclerosis, and then to a higher risk of heart disease first became apparent in the literature. As regulatory agencies and scientists continually found this association, food companies became prompted to come up with no-saturated fat alternatives. No-fat foods, low-fat foods, and foods with substituted fats have appeared in ample quantities on grocery store shelves. In fact, over 15,000 such products have been promoted over the past several decades.

Excessive consumption of saturated fats can negatively affect your health since the fat you eat in your diet gets directly into your cell membranes. This valid concern about saturated fats has been generalized to all fats, however, and your body needs other fats. Saturated fats are primarily found in high amounts in processed foods and meat products, in particular the meats that have white, solid fat on them. In addition, the fats found in meat fats also include cholesterol, so diets high in fatty meat are also high in cholesterol.

Minimizing the consumption of saturated fats is a good idea, but minimizing the consumption of all fats is not. Consider that your brain is approximately 70 percent fat. In addition, diets low in all types of fats have been associated with increased risk of hormone abnormalities, cardiovascular disease, and decreased brain and immune function. So, the real question is not

how to indiscriminately avoid all fats, but which fats, in which amounts are good for you?

The Health Promoting Fats: Monounsaturated and Polyunsaturated Fats

Monounsaturated Fats

Monounsaturated fats caught the attention of research scientists after they first notcied that people who eat a traditional Mediterranean diet have a lower risk of developing cardiovascular disese, certain types of cancer, and rheumatoid arthritis. Traditional Mediterranean diets contain high amounts of olive oil, which is high in oleic acid, a monounsaturated fatty acid. Other monounsaturated fats include myristoleic and palmitoleic acids. In addition to olive oil, other food sources for monounsaturated fatty acids include canola oil, avocadoes, almonds, and cashews.

Research continues to support the theory that diets high in monounsaturated fats are health-promoting; however, the most exciting latest research revolves around the polyunsaturated fats, in particular, the omega-3 fatty acids.

The Health Promoting Polyunsaturated Fats

The polyunsaturated fats (PUFA) are molecules that contain many unsaturated bonds, a characteristic which distinguishes them chemically from the other fats. In practical terms, this chemical structure is the reason these fats are liquid even when cold. Many different polyunsaturated fats exist, but the ones getting the most attention from research scientists are the essential fats, linolenic acid and alpha-linoleic acid, and the omega-3 fatty acids.

The Essential PUFA Fats

Your body can make all the different fats it needs from two starting molecules, the two essential fats: linoleic acid (an omega-6 fatty acid) and alpha-linolenic acid (an omega-3 fatty acid). Because these are essential fats, meaning your body can't make them, you must get them from your diet. All other PUFAs can be made from these fats. The omega-6 PUFAs, such as arachidonic acid, one of the major fats in your cell membranes, are made from linoleic acid. The omega-3 fats, such as docosahexaenoic acid, the main fat in your brain, are made from alpha-linolenic acid.

Linoleic acid is an omega-6 fatty acid which is plentiful in the diet of most Americans. This fat is found in at high levels in oils from grains, nuts and legumes, and is often provided in your diet by sunflower, safflower, sesame, corn, soy, and peanut oils. In the body, linoleic acid is first converted to another omega-6 fat called gamma-linolenic acid, which is also found in evening primrose oil and borage oil.

As mentioned, few people are deficient in the omega-6 essential fat, linoleic acid; this is, in part, because arachidonic acid, which is made from linoleic acid, is found at high levels in animal tissue, such as beef and poultry. Since the average Western diet contains a lot of meat, most people get high quantities of arachionic acid.

The omega-3 fats, which are produced in your body from the essential omega-3 fat -- alpha linolenic acid -- have generated much interest since studies continue to show that diets low in omega-3 fats are associated with many health diseases including chronic inflammatory conditions like rheumatoid arthritis, inflammatory bowel disease, and cardiovascular disease, and behavioral syndromes like ADHD (attention deficit hyperactivity disorder). Alpha-linolenic acid is found in high quantities in flax oil, canola oil, and some leafy vegetables. Some of the most important omega-3 fats, which are synthesized from alpha-linolenic acid, are docosahaenoic acid (DHA) and eicosapentaenoic acid (EPA), and these can be obtained directly from the diet as well. Excellent sources for EPA and DHA are fish and algae.

Although omega-6 fats, like arachidonic acid, play important roles in your body, consuming too many of these in comparison to the amount of omega-3 fats you consume can cause problems. This is because the fluidity, or flexibility of cell membranes is so dependent on having a variety of fats present. Since omega-6 fats are in such high quantities in most people's diets, they occupy places where omega-3 fats should be. For good health, it is vital to consider the ratio of omega-6 to omega-3 fats in your diet.

The proper balance of omega-3 to omega-6 is extremely important not only for healthy cell membranes, but also because omega-6 fats are the precursors for pro-inflammatory molecules--the molecules that promote and maintain inflammatory reactions. Omega-3 fats, in contrast, are the precursors for anti-inflammatory molecules. Inflammatory reactions are an integral part of they way your body protects you against infections and promotes healing, but the body must be able to turn off its inflammatory defenses when their work is done. This is one of the primary roles of the omega-3 fats. When you lack a balance of omega-3 to omega-6 fats, your body can't turn off these inflammatory reactions, which promotes conditions of chronic inflammation. Current research continues to support that diseases such as atherosclerosis, arthritis, inflammatory bowel disese, and asthma are perpetuated by a heightened inflammatory state, and that in individuals with these conditions, the pro-inflammatory omega-6 essential fats are not balanced by adequate amounts of the anti-inflammatory omega-3s.

The ideal ratio of omega-3 to omega-6 is not known, but is estimated to be around 1:2; whereas, the current ratio in the typical American diet is more like 1:25. In order to achieve a more beneficial ratio, it is important to decrease the amount of omega-6 fatty acids in your diet, while increasing the amount of omega-3 fatty acids like EPA, DHA, and alpha-linolenic acid. This can be accomplished by reducing your comsumption of meats, dairy products, and refined foods, while increasing consumption of the omega-3 rich foods such as wild-caught cold-water fish like salmon, flaxseed oil, walnuts, and leafy green vegetables.

Conclusion

Macronutrients serve as building blocks for all the vital molecules in your body. Healthy fats, in particular, provide balance for inflammation reactions and keep your cell membranes healthy. The World's Healthiest Foods provide complex carbohydrates, essential fats, and proteins that feature not just a sufficient quantity of these macronutrients, but also the full spectrum of health-promoting compounds associated with these macronutrients, while minimizing those that appear to provide less benefit. Another important reason to choose the World's Healthiest Foods as your source of macronutrients is that in these foods, the macronutrient molecules are not alone, they are complexed with the full array of vitamins, minerals, and phytonutrients. It is the interplay among this full range of nutrients that orchestrates not merely the absence of disease, but optimal vitality and healthy aging.

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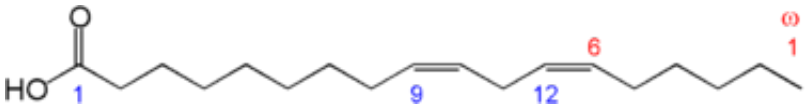
ANNEX AC:

"Omega-6 fatty acid" Wikipedia, accessed March 5, 2018

WIKIPEDIA

Omega-6 fatty acid

Omega-6 fatty acids (also referred to as **ω-6 fatty acids** or ***n*-6 fatty acids**) are a family of pro-inflammatory and anti-inflammatory polyunsaturated fatty acids[1] that have in common a final carbon-carbon double bond in the *n*-6 position, that is, the sixth bond, counting from the methyl end.[2]



The chemical structure of linoleic acid, a common omega-6 fatty acid found in many nuts, seeds and vegetable oils.

The biological effects of the omega-6 fatty acids are largely produced during and after physical activity for the purpose of promoting growth and during the inflammatory cascade to halt cell damage and promote cell repair by their conversion to omega-6 eicosanoids that bind to diverse receptors found in every tissue of the body.

Contents

Biochemistry

Linoleic acid (18:2, *n*−6), the shortest-chained omega-6 fatty acid, is one of many essential fatty acids and is categorized as an essential fatty acid because the human body cannot synthesize it. Mammalian cells lack the enzyme omega-3 desaturase and therefore cannot convert omega-6 fatty acids to omega-3 fatty acids. Closely related omega-3 and omega-6 fatty acids act as competing substrates for the same enzymes.[3] This outlines the importance of the proportion of omega-3 to omega-6 fatty acids in a diet.[3]

Omega-6 fatty acids are precursors to endocannabinoids, lipoxins, and specific eicosanoids.

Medical research on humans found a correlation (though correlation does not imply causation) between the high intake of omega-6 fatty acids from vegetable oils and disease in humans. However, biochemistry research has concluded that air pollution, heavy metals, smoking, passive smoking, lipopolysaccharides, lipid peroxidation products (found mainly in vegetable oils, roasted nuts and roasted oily seeds) and other exogenous toxins initiate the inflammatory response in the cells which leads to the expression of the COX-2 enzyme and subsequently to the temporary production of inflammatory *promoting* prostaglandins from arachidonic acid for the purpose of alerting the immune system of the cell damage and eventually to the production of anti-inflammatory molecules (e.g. lipoxins & prostacyclin) during the resolution phase of inflammation, after the cell damage has been repaired.[4][5][6][7][8][9][10][11][12][13][14][15]

Pharmacology

The conversion of cell membrane arachidonic acid (20:4n-6) to omega-6 prostaglandin and omega-6 leukotriene eicosanoids during the inflammatory cascade provides many targets for pharmaceutical drugs to impede the inflammatory process in atherosclerosis,[16] asthma, arthritis, vascular disease, thrombosis, immune-inflammatory processes, and tumor proliferation. Competitive interactions with the omega-3 fatty acids affect the relative storage, mobilization, conversion and action of the omega-3 and omega-6 eicosanoid precursors (see Essential fatty acid interactions).

Suggested negative health effects

Some medical research suggests that excessive levels of omega-6 fatty acids from seed oils relative to certain omega-3 fatty acids may increase the probability of a number of diseases.[17][18][19]

Modern Western diets typically have ratios of omega-6 to omega-3 in excess of 10 to 1, some as high as 30 to 1; the average ratio of omega-6 to omega-3 in the Western diet is 15:1–16.7:1.[16] Humans are thought to have evolved with a diet of a 1-to-1 ratio of omega-6 to omega-3 and the optimal ratio is thought to be 4 to 1 or lower,[16] although some sources suggest ratios as low as 1:1.[20] A ratio of 2–3:1 omega 6 to omega 3 helped reduce inflammation in patients with rheumatoid arthritis.[16] A ratio of 5:1 had a beneficial effect on patients with asthma but a 10:1 ratio had a negative effect.[16] A ratio of 2.5:1 reduced rectal cell proliferation in patients with colorectal cancer, whereas a ratio of 4:1 had no effect.[16]

Excess omega-6 fatty acids from vegetable oils interfere with the health benefits of omega-3 fats, in part because they compete for the same rate-limiting enzymes. A high proportion of omega-6 to omega-3 fat in the diet shifts the physiological state in the tissues toward the pathogenesis of many diseases: prothrombotic, proinflammatory and proconstrictive.[21]

Chronic excessive production of omega-6 eicosanoids is correlated with arthritis, inflammation, and cancer. Many of the medications used to treat and manage these conditions work by blocking the effects of the COX-2 enzyme.[22] Many steps in formation and action of omega-6 prostaglandins from omega-6 arachidonic acid proceed more vigorously than the corresponding competitive steps in formation and action of omega-3 hormones from omega-3 eicosapentaenoic acid.[23] The COX-1 and COX-2 inhibitor medications, used to treat inflammation and pain, work by preventing the COX enzymes from turning arachidonic acid into inflammatory compounds.[24] (See Cyclooxygenase for more information.) The LOX

inhibitor medications often used to treat asthma work by preventing the LOX enzyme from converting arachidonic acid into the leukotrienes.[25][26] Many of the anti-mania medications used to treat bipolar disorder work by targeting the arachidonic acid cascade in the brain.[27]

A high consumption of oxidized polyunsaturated fatty acids (PUFAs), which are found in most types of vegetable oil, may increase the likelihood that postmenopausal women will develop breast cancer.[28] Similar effect was observed on prostate cancer, but the study was performed on mice.[29] Another "analysis suggested an inverse association between total polyunsaturated fatty acids and breast cancer risk, but individual polyunsaturated fatty acids behaved differently [from each other]. [...] a 20:2 derivative of linoleic acid [...] was inversely associated with the risk of breast cancer".[30]

Omega-6 consumption

Industry-sponsored studies have suggested that omega-6 fatty acids should be consumed in a 1:1 ratio to omega-3,[31] though it has been observed that the diet of many individuals today is at a ratio of about 16:1, mainly from vegetable oils.[31] Omega-6 and omega-3 are essential fatty acids that are metabolized by some of the same enzymes, and therefore an imbalanced ratio can affect how the other is metabolized.[32] In a study performed by Ponnampalam,[33] it was noticed that feeding systems had a great effect on nutrient content on the meat sold to consumers. Cynthia Doyle conducted an experiment to observe the fatty acid content of beef raised through grass feeding versus grain feeding; she concluded that grass fed animals contain an overall omega-6:omega-3 ratio that is preferred by nutritionists.[32] In today's modern agriculture, the main focus is on production quantity, which has decreased the omega-3 content, and increased the omega-6 content, due to simple changes such as grain-feeding cattle.[16] In grain-feeding cattle, this is a way to increase their weight and prepare them for slaughter much quicker compared to grass-feeding. This modern way of feeding animals may be one of many indications as to why the omega-6:omega-3 ratio has increased.

List of omega-6 fatty acids

Common name	Lipid name	Chemical name
Linoleic acid (LA)	18:2 (*n*–6)	*all-cis*-9,12-octadecadienoic acid
Gamma-linolenic acid (GLA)	18:3 (*n*–6)	*all-cis*-6,9,12-octadecatrienoic acid
Calendic acid	18:3 (*n*–6)	8E,10E,12Z-octadecatrienoic acid
Eicosadienoic acid	20:2 (*n*–6)	*all-cis*-11,14-eicosadienoic acid
Dihomo-gamma-linolenic acid (DGLA)	20:3 (*n*–6)	*all-cis*-8,11,14-eicosatrienoic acid
Arachidonic acid (AA, ARA)	20:4 (*n*–6)	*all-cis*-5,8,11,14-eicosatetraenoic acid
Docosadienoic acid	22:2 (*n*–6)	*all-cis*-13,16-docosadienoic acid
Adrenic acid	22:4 (*n*–6)	*all-cis*-7,10,13,16-docosatetraenoic acid
Osbond acid	22:5 (*n*–6)	*all-cis*-4,7,10,13,16-docosapentaenoic acid
Tetracosatetraenoic acid	24:4 (*n*–6)	*all-cis*-9,12,15,18-tetracosatetraenoic acid
Tetracosapentaenoic acid	24:5 (*n*–6)	*all-cis*-6,9,12,15,18-tetracosapentaenoic acid

It is interesting to note that melting point of the fatty acids increase as the number of carbons in the chain increases.

Dietary linoleic acid requirement

Adding more controversy to the omega-6 fat issue is that the dietary requirement for linoleic acid has been questioned, because of a significant methodology error proposed by University of Toronto scientist Stephen Cunnane.[34] Cunnane proposed that the seminal research used to determine the dietary requirement for linoleic acid was based on feeding animals linoleic acid-deficient diets, which were simultaneously deficient in omega-3 fats. The omega-3 deficiency was not taken into account. The omega-6 oils added back systematically to correct the deficiency also contained trace amounts of omega-3 fats. Therefore, the researchers were inadvertently correcting the omega-3 deficiency as well. Ultimately, it took more oil to correct both deficiencies. According to Cunnane, this error overestimates linoleic acid requirements by 5 to 15 times.

Dietary sources

Four major food oils (palm, soybean, rapeseed, and sunflower) provide more than 100 million metric tons annually, providing more than 32 million metric tons of omega-6 linoleic acid and 4 million metric tons of omega-3 alpha-linolenic acid.[35]

Dietary sources of omega-6 fatty acids include:[36]

- poultry
- eggs
- nuts
- hulled sesame seeds
- cereals

- durum wheat
- whole-grain breads
- most vegetable oils
- grape seed oil
- evening primrose oil
- borage oil
- blackcurrant seed oil
- flax/linseed oil
- rapeseed or canola oil
- hemp oil
- soybean oil
- cottonseed oil
- sunflower seed oil
- corn oil
- safflower oil
- pumpkin seeds

The evening primrose flower (*O. biennis*) produces an oil containing a high content of γ-linolenic acid, a type of omega-6 fatty acid.

See also

- Essential fatty acid interactions
- Essential nutrients
- Linolenic acid
- Omega-3 fatty acid
- Omega-7 fatty acid
- Omega-9 fatty acid
- Wheat germ oil
- Lipid peroxidation
- Inflammation
- Cattle feeding
- Olive oil regulation and adulteration
- Ratio of fatty acids in different foods

Notes and references

1. JZ, Nowak (2010). "Anti-inflammatory pro-resolving derivatives of omega-3 and omega-6 polyunsaturated fatty acids". *Postepy higieny i medycyny doswiadczalnej (Online)*. **64**: 115–32. PMID 20354260 (https://www.ncbi.nlm.nih.gov/pubmed/20354260).
2. Chow, Ching Kuang (2001). *Fatty Acids in Foods and Their Health Implications*. New York: Routledge Publishing. OCLC 25508943 (https://www.worldcat.org/oclc/25508943).
3. Bibus, Doug; Lands, Bill (April 18, 2015). "Balancing proportions of competing omega-3 and omega-6 highly unsaturated fatty acids (HUFA) in tissue lipids". *Prostaglandins Leukot. Essent. Fatty Acids*. **99**: 19–23. doi:10.1016/j.plefa.2015.04.005 (https://doi.org/10.1016%2Fj.plefa.2015.04.005). PMID 26002802 (https://www.ncbi.nlm.nih.gov/pubmed/26002802).
4. Ricciotti, Emanuela; FitzGerald,, Garret A. (2011). "Prostaglandins and inflammation" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3021099). *American Heart Association Journal*. **31** (5): 986–1000.

mc/articles/PMC3081099). *American Heart Association Journal*. **31** (5): 986–1000. doi:10.1161/ATVBAHA.110.207449 (https://doi.org/10.1161%2FATVBAHA.110.207449). PMC 3081099 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3081099). PMID 21508345 (https://www.ncbi.nlm.nih.gov/pubmed/21508345).

5. Zhao, Yutong; Usatyuk, Peter V.; Gorshkova, Irina A.; He, Donghong; Wang, Ting; Moreno-Vinasco, Liliana; Geyh, Alison S.; Breysse, Patrick N.; et al. (2009). "Regulation of COX-2 Expression and IL-6 Release by Particulate Matter in Airway Epithelial Cells". *American Journal of Respiratory Cell and Molecular Biology*. **40** (1): 19–30. doi:10.1165/rcmb.2008-0105OC (https://doi.org/10.1165%2Frcmb.2008-0105OC). PMID 18617679 (https://www.ncbi.nlm.nih.gov/pubmed/18617679).
6. Calderón-Garcidueñas, Lilian; Reed, William; Maronpot, Robert; Henriquez-Roldán, Carlos; Delgado-Chavez, Ricardo; Carlos Henriquez-Roldán, Ana; Dragustinovis, Irma; Franco-Lira, Maricela; et al. (2004). "Brain Inflammation and Alzheimer's-Like Pathology in Individuals Exposed to Severe Air Pollution". *Toxicologic Pathology*. **32** (6): 650–8. doi:10.1080/01926230490520232 (https://doi.org/10.1080%2F01926230490520232). PMID 15513908 (https://www.ncbi.nlm.nih.gov/pubmed/15513908).
7. Moraitis, Dimitrios; Du, Baoheng; De Lorenzo, Mariana S.; Boyle, Jay O.; Weksler, Babette B.; Cohen, Erik G.; Carew, John F.; Altorki, Nasser K.; et al. (2005). "Levels of Cyclooxygenase-2 Are Increased in the Oral Mucosa of Smokers: Evidence for the Role of Epidermal Growth Factor Receptor and Its Ligands" (http://cancerres.aacrjournals.org/cgi/pmidlookup?view=long&pmid=15695412). *Cancer Research*. **65** (2): 664–70. PMID 15695412 (https://www.ncbi.nlm.nih.gov/pubmed/15695412).
8. Yang, Chuen-Mao; Lee, I-Ta; Lin, Chih-Chung; Yang, Ya-Lin; Luo, Shue-Fen; Kou, Yu Ru; Hsiao, Li-Der (2009). "Cigarette smoke extract induces COX-2 expression via a PKCα/c-Src/EGFR, PDGFR/PI3K/Akt/NF-κB pathway and p300 in tracheal smooth muscle cells". *American Journal of Physiology. Lung Cellular and Molecular Physiology*. **297** (5): L892–902. doi:10.1152/ajplung.00151.2009 (https://doi.org/10.1152%2Fajplung.00151.2009). PMID 19717552 (https://www.ncbi.nlm.nih.gov/pubmed/19717552).
9. Martey, Christine A.; Stephen J., Pollock; Chantal K., Turner; Katherine M. A., O'Reilly; Carolyn J., Baglole; Richard P., Phipps; Patricia J., Sime (2004). "Cigarette smoke induces cyclooxygenase-2 and microsomal prostaglandin E2 synthase in human lung fibroblasts: Implications for lung inflammation and cancer". *American Journal of Physiology. Lung Cellular and Molecular Physiology*. **287** (5): L981–91. doi:10.1152/ajplung.00239.2003 (https://doi.org/10.1152%2Fajplung.00239.2003). PMID 15234907 (https://www.ncbi.nlm.nih.gov/pubmed/15234907).
10. Font-Nieves, Miriam; Sans-Fons, M. Glòria; Gorina, Roser; Bonfill-Teixidor, Ester; Salas-Pérdomo, Angélica; Márquez-Kisinousky, Leonardo; Santalucia, Tomàs; M. Planas, Anna (2012). "Induction of COX-2 enzyme and down-regulation of COX-1 expression by lipopolysaccharide (LPS) control prostaglandin E2 production in astrocytes" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3307308). *The Journal of Biological Chemistry*. **287** (9): 6454–6468. doi:10.1074/jbc.M111.327874 (https://doi.org/10.1074%2Fjbc.M111.327874). PMC 3307308 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3307308). PMID 22219191 (https://www.ncbi.nlm.nih.gov/pubmed/22219191).
11. Ren, Rendong; Hashimoto, Takashi; Mizuno, Masashi; Takigawa, Hirosato; Yoshida, Masaru; Azuma, Takeshi; Kanazawa, Kazuki (2013). "A lipid peroxidation product 9-oxononanoic acid induces phospholipase A2 activity and thromboxane A2 production in human blood" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3652295). *Journal of Clinical Biochemistry and Nutrition*. **52** (3): 228–233. doi:10.3164/jcbn.12-110 (https://doi.org/10.3164%2Fjcbn.12-110). PMC 3652295 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3652295). PMID 23704812 (https://www.ncbi.nlm.nih.gov/pubmed/23704812).
12. Olszowski, Tomasz (2015). "The Effect of Cadmium on COX-1 and COX-2 Gene, Protein Expression, and Enzymatic Activity in THP-1 Macrophages" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4424267). *Biological Trace Element Research*. **165** (2): 135–144. doi:10.1007/s12011-015-0234-6 (https://doi.org/10.1007%2Fs12011-015-0234-6). PMC 4424267 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4424267). PMID 25645360 (https://www.ncbi.nlm.nih.gov/pubmed/25645360).
13. Sun Youn, Hyung (2011). "Mercury induces the expression of cyclooxygenase-2 and inducible nitric oxide synthase".

Biomedical Laboratory Science. **29** (2): 169–174. doi:10.1177/0748233711427048 (https://doi.org/10.1177%2F0748233711427048). PMID 22080037 (https://www.ncbi.nlm.nih.gov/pubmed/22080037).

14. Wei, Jinlong (2014). "Lead induces COX-2 expression in glial cells in a NFAT-dependent, AP-1/NFκB-independent manner" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4238429). *Toxicology*. **325**: 67–73. doi:10.1016/j.tox.2014.08.012 (https://doi.org/10.1016%2Fj.tox.2014.08.012). PMC 4238429 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4238429). PMID 25193092 (https://www.ncbi.nlm.nih.gov/pubmed/25193092).
15. J, He (2014). "Chronic arsenic exposure and angiogenesis in human bronchial epithelial cells via the ROS/miR-199a-5p/HIF-1α/COX-2 pathway" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3948041). *Environ Health Perspect*. **122** (1): 255–261. doi:10.1289/ehp.1307545 (https://doi.org/10.1289%2Fehp.1307545). PMC 3948041 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3948041). PMID 24413338 (https://www.ncbi.nlm.nih.gov/pubmed/24413338).
16. Simopoulos, A.P (2002). "The importance of the ratio of omega-6/omega-3 essential fatty acids". *Biomedicine & Pharmacotherapy*. **56** (8): 365–79. doi:10.1016/S0753-3322(02)00253-6 (https://doi.org/10.1016%2FS0753-3322%2802%2900253-6). PMID 12442909 (https://www.ncbi.nlm.nih.gov/pubmed/12442909).
17. Lands, W. E.M. (2005). "Dietary Fat and Health: The Evidence and the Politics of Prevention: Careful Use of Dietary Fats Can Improve Life and Prevent Disease". *Annals of the New York Academy of Sciences*. **1055**: 179–92. Bibcode:2005NYASA1055..179L (http://adsabs.harvard.edu/abs/2005NYASA1055..179L). doi:10.1196/annals.1323.028 (https://doi.org/10.1196%2Fannals.1323.028). PMID 16387724 (https://www.ncbi.nlm.nih.gov/pubmed/16387724).
18. Hibbeln, Joseph R; Nieminen, Levi RG; Blasbalg, Tanya L; Riggs, Jessica A; Lands, William EM (2006). "Healthy intakes of n–3 and n–6 fatty acids: estimations considering worldwide diversity" (http://www.ajcn.org/cgi/pmidlookup?view=long&pmid=16841858). *The American Journal of Clinical Nutrition*. **83** (6 Suppl): 1483S–1493S. PMID 16841858 (https://www.ncbi.nlm.nih.gov/pubmed/16841858).
19. Okuyama, H.; Ichikawa, Y.; Sun, Y.; Hamazaki, T.; Lands, W.E.M. (2006). "ω3 Fatty Acids Effectively Prevent Coronary Heart Disease and Other Late-Onset Diseases – The Excessive Linoleic Acid Syndrome". In Okuyama, H. *Prevention of Coronary Heart Disease*. World Review of Nutrition and Dietetics. pp. 83–103. doi:10.1159/000097809 (https://doi.org/10.1159%2F000097809). ISBN 3-8055-8179-3. PMID 17167282 (https://www.ncbi.nlm.nih.gov/pubmed/17167282).
20. Lands, WEM (2005). *Fish, Omega 3 and human health*. American Oil Chemists' Society. ISBN 978-1-893997-81-3.
21. Simopoulos, A.P. (2003). "Importance of the Ratio of Omega-6/Omega-3 Essential Fatty Acids: Evolutionary Aspects" (https://books.google.com/books?id=_0PWAie_YIkC&pg=PA1). In Simopoulos, Artemis P.; Cleland, Leslie G. *Omega-6/Omega-3 Essential Fatty Acid Ratio: The Scientific Evidence*. World Review of Nutrition and Dietetics. **92**. pp. 1–22. doi:10.1159/000073788 (https://doi.org/10.1159%2F000073788). ISBN 3-8055-7640-4. PMID 14579680 (https://www.ncbi.nlm.nih.gov/pubmed/14579680).
22. Smith, William L. (2008). "Nutritionally essential fatty acids and biologically indispensable cyclooxygenases". *Trends in Biochemical Sciences*. **33** (1): 27–37. doi:10.1016/j.tibs.2007.09.013 (https://doi.org/10.1016%2Fj.tibs.2007.09.013). PMID 18155912 (https://www.ncbi.nlm.nih.gov/pubmed/18155912).
23. Wada, M.; Delong, C. J.; Hong, Y. H.; Rieke, C. J.; Song, I.; Sidhu, R. S.; Yuan, C.; Warnock, M.; et al. (2007). "Enzymes and Receptors of Prostaglandin Pathways with Arachidonic Acid-derived Versus Eicosapentaenoic Acid-derived Substrates and Products". *Journal of Biological Chemistry*. **282** (31): 22254–66. doi:10.1074/jbc.M703169200 (https://doi.org/10.1074%2Fjbc.M703169200). PMID 17519235 (https://www.ncbi.nlm.nih.gov/pubmed/17519235).
24. Cleland, Leslie G; James, Michael J; Proudman, Susanna M (2006). "Fish oil: what the prescriber needs to know" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1526555). *Arthritis Research & Therapy*. **8** (1): 202. doi:10.1186/ar1876 (https://doi.org/10.1186%2Far1876). PMC 1526555 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1526555). PMID 16542466 (https://www.ncbi.nlm.nih.gov/pubmed/16542466).

25. Mickleborough, Timothy (2005). "Dietary Omega-3 Polyunsaturated Fatty Acid Supplementation and Airway Hyperresponsiveness in Asthma". *Journal of Asthma*. **42** (5): 305–14. doi:10.1081/JAS-62950 (https://doi.org/10.1081%2FJAS-62950). PMID 16036405 (https://www.ncbi.nlm.nih.gov/pubmed/16036405).
26. K S Broughton; Johnson, CS; Pace, BK; Liebman, M; Kleppinger, KM (1997-04-01). "Reduced asthma symptoms with n-3 fatty acid ingestion are related to 5-series leukotriene production" (http://www.ajcn.org/cgi/pmidlookup?view=long&pmid=9094887). *The American Journal of Clinical Nutrition*. **65** (4): 1011–7. PMID 9094887 (https://www.ncbi.nlm.nih.gov/pubmed/9094887).
27. Lee, Ho-Joo; Rao, Jagadeesh S.; Rapoport, Stanley I.; Bazinet, Richard P. (2007). "Antimanic therapies target brain arachidonic acid signaling: Lessons learned about the regulation of brain fatty acid metabolism". *Prostaglandins, Leukotrienes and Essential Fatty Acids*. **77** (5–6): 239–46. doi:10.1016/j.plefa.2007.10.018 (https://doi.org/10.1016%2Fj.plefa.2007.10.018). PMID 18042366 (https://www.ncbi.nlm.nih.gov/pubmed/18042366).
28. Sonestedt, Emily; Ericson, Ulrika; Gullberg, Bo; Skog, Kerstin; Olsson, Håkan; Wirfält, Elisabet (2008). "Do both heterocyclic amines and omega-6 polyunsaturated fatty acids contribute to the incidence of breast cancer in postmenopausal women of the Malmö diet and cancer cohort?". *International Journal of Cancer*. **123** (7): 1637–43. doi:10.1002/ijc.23394 (https://doi.org/10.1002%2Fijc.23394). PMID 18636564 (https://www.ncbi.nlm.nih.gov/pubmed/18636564).
29. Yong Q. Chen, at al; Min; Wu; Wu; Perry; Cline; Thomas; Thornburg; Kulik; Smith; Edwards; d'Agostino; Zhang; Wu; Kang; Chen (2007). "Modulation of prostate cancer genetic risk by omega-3 and omega-6 fatty acids" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1890998). *The Journal of Clinical Investigation*. **117** (7): 1866–1875. doi:10.1172/JCI31494 (https://doi.org/10.1172%2FJCI31494). PMC 1890998 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1890998). PMID 17607361 (https://www.ncbi.nlm.nih.gov/pubmed/17607361).
30. Pala, Valeria; Krogh, Vittorio; Muti, Paola; Chajès, Véronique; Riboli, Elio; Micheli, Andrea; Saadatian, Mitra; Sieri, Sabina; Berrino, Franco (2001). "Erythrocyte Membrane Fatty Acids and Subsequent Breast Cancer: A Prospective Italian Study". *Journal of the National Cancer Institute*. **93** (14): 1088–95. doi:10.1093/jnci/93.14.1088 (https://doi.org/10.1093%2Fjnci%2F93.14.1088). PMID 11459870 (https://www.ncbi.nlm.nih.gov/pubmed/11459870).
31. Simopoulos, A.P (28 July 2006). "Evolutionary aspects of diet, the omega-6/omega-3 ratio and genetic variation: nutritional implications for chronic diseases" (http://www.nutrasource.ca/files/omega_3_chronic_nov2006.pdf) (PDF). *Biomedicine & Pharmacotherapy*. **60** (9): 502–507. doi:10.1016/j.biopha.2006.07.080 (https://doi.org/10.1016%2Fj.biopha.2006.07.080). Retrieved 8 February 2015.
32. Doyle, Cynthia; Abbott, Amber; Doyle, Patrick; Nader, Glenn; Larson, Stephanie (2010). "A review of fatty acid profiles and antioxidant content in grass-fed and grain-fed beef" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2846864). *Nutrition Journal*. **9** (1): 10. doi:10.1186/1475-2891-9-10 (https://doi.org/10.1186%2F1475-2891-9-10). PMC 2846864 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2846864). PMID 20219103 (https://www.ncbi.nlm.nih.gov/pubmed/20219103).
33. Ponnampalam, Eric; Mann, Neil; Sinclair, Andrew (2006). "Effect of feeding systems on omega-3 fatty acids, conjugated linoleic acid and trans fatty acids in Australian beef cuts: potential impact on human health" (http://apjcn.nhri.org.tw/server/APJCN/15/1/21.pdf) (PDF). *Asia Pac J Clin Nutr*. **15** (1): 21–29. PMID 16500874 (https://www.ncbi.nlm.nih.gov/pubmed/16500874). Retrieved 8 February 2015.
34. Cunnane, Stephen C. (2003). "Problems with essential fatty acids: Time for a new paradigm?". *Progress in Lipid Research*. **42** (6): 544–68. doi:10.1016/S0163-7827(03)00038-9 (https://doi.org/10.1016%2FS0163-7827%2803%2900038-9). PMID 14559071 (https://www.ncbi.nlm.nih.gov/pubmed/14559071).
35. Gunstone, Frank (December 2007). "Market update: Palm oil" (http://www.highbeam.com/doc/1P3-1421893231.html). *International News on Fats, Oils and Related Materials*. **18** (12): 835–6.
36. "Food sources of total omega 6 fatty acids" (http://riskfactor.cancer.gov/diet/foodsources/fatty_acids/table2.html). Retrieved 2011-09-04.

Additional sources

- Tokar, Steve (2005-09-02). "Omega-6 fatty acids cause prostate tumor cell growth in culture" (http://www.medicalnewstoday.com/articles/29976.php). *Medical News Today*. MediLexicon International. Retrieved 2008-03-23.
- "Brain fatty acid levels linked to depression" (http://www.news-medical.net/?id=10398). *News-Medical.Net*. AZoNetwork. 2005-05-25. Retrieved 2008-03-23.
- Tribole, E.F. (2006-03-27). "Excess Omega-6 Fats Thwart Health Benefits from Omega-3 Fats" (http://www.bmj.com/rapid-response/2011/10/31/excess-omega-6-fats-thwart-health-benefits-omega-3-fats). *British Medical Journal Rapid Responses to Hooper, et al., 2006*. **332** (7544): 752. Retrieved 2008-03-23.
- Erasmus, Udo (1993). *Fats That Heal, Fats That Kill* (3rd ed.). Burnaby (BC): Alive Books. ISBN 978-0-920470-38-1.

ANNEX AD:

Petition to the Administrative Council of the European Patent Organization, August 10, 2019
(Attachments omitted, which are available at
https://register.epo.org/application?number=EP09735962
and
https://register.epo.org/application?number=EP17182663)

August 10, 2019 **BY EMAIL**

Petition to the Administrative Council of the European Patent Organization

Cc:
Antonio Campinos, President of the EPO
Christoph Ernst, VP Legal/ International Affairs
Karin Seegert, COO, Healthcare & Chemistry
Piotr Wierzejewski, Quality Management
Stoyan Radkov - Applicant's Representative
Tim Moss, CEO, Intellectual Property Office of the United Kingdom
Vincentia Rosen-Sandiford, Director, Netherlands Patent Office
Emmanuel Macron, President, French Republic
Angela Merkel, Chancellor, Germany
Mark Rutte, Prime Minister, The Netherlands
Boris Johnson, Prime Minister, United Kingdom
Cornelia Rudloff-Schäffer, President, German PTO
Cadre Philippe, Director, French National Institute of Industrial Property

Re: European patent application 09735962.4; and European divisional application 17182663.9; Applicant: Asha Nutrition Sciences, Inc.

Dear Delegates in the Administrative Council,

We have been prosecuting the referenced patent applications directed to critical innovations for public health at EPO for last 10 years. However, rather than advancing the innovations EPO has been obstructing them. EPO statements in the prosecution history evidence that rejections have been applied to oblige us to reduce the claimed scope, even though as per provisions of European Patent Convention, the subject claims are perfectly patentable.

A narrow patent is not synonymous with a quality patent. The metric of quality disregarded by EPO is genuine innovation, *measured by betterment of life achieved*, though that is the very purpose of patents and is built into the law. For example, solutions to critical unmet needs are inventive even if claims are otherwise obvious (GL[1], G-VII, 10.3). Narrow patents in the nutrition arts have already caused great harm to public health and created *patent-practice-made humanitarian crises* by creating misinformation and taken us farther away from solving nutritional problems, preventative solutions, and sustainability. Narrow patent would defeat the very purpose of the subject innovations, conceived to overcome the misinformation in the art and the resulting public suffering and to set humanity on course to long-term solution to the lipid problem sparking downstream advancements in public health. Without sufficient patent scope and term, it is impracticable to effectively implement the claimed solutions.

EPO's unchecked dominance over European Patents results in *obstruction of innovation and fosters stagnation*. The dominance creates perverse incentives, such as EPO colluding with patent lawyers to defraud public, inventors, and applicants. As supervisory body of the EPO, we request your review of the matter detailed below and provide requested relief.

[1] Guidelines for Examination in the European Patent Office, November 2018

TABLE OF CONTENTS

ATTACHMENTS: Pages

I. Background of the Applications

The parent application has a filing date of 20 April 2009, it entered European phase on November 19, 2010. After the Examining Division (hereinafter "ED-1") failed to render justice, the case was appealed to the Boards of Appeal (hereinafter "BoA"). At the oral proceedings held in July 2017, BoA colluded with the Applicant's own representative (Representative 1) to undermine the application. Request for Correction of Minutes dated 3 August 2017 was submitted on 20 December 2017 (Attachments B and C). Formal Complaint was filed with EPO on January 30, 2018 (Attachment A with Exhibits A-E), which was dismissed by Directorate Quality Management. A Petition under Article 112a for review by the Enlarged Board of Appeal (hereinafter "EBoA") was filed on March 26, 2018 (Attachment D), with the Complaint and copy of email communications between the Applicant and Representative 1 (Exhibit C) and declaration from Applicant's CEO evidencing improper conduct at the oral proceedings (Exhibit D). The response to EBoA communication was filed on July 22, 2018 (Attachments E and F). The Enlarged Board disregarded the evidence of wrongdoings (Exhibits C-D) and refused to grant a review on October 10, 2018 (Attachment G). The Applicant documented in the Formal Complaint filed on November 12, 2018 (Attachment H) that it was improper for EBoA to disregard the evidence Exhibits C-D, which are the only mechanisms available to Applicant to report wrongdoings at EPO oral proceedings.

The divisional application filed in 2017 is now under examination by new Examining Division (hereinafter "ED-2"). ED-2 appears to take BoA and EBoA improprieties in the parent case as license for more improprieties in the divisional case (discussed below).

II. Background of the Inventions

The innovations pertain to tailored delivery of lipids. The independent claims pending in the divisional application are as follows (similar claims were presented in the parent case).

Claim 1:

A lipid-containing formulation for a subject, comprising a mixture of lipids from different sources and a dosage of omega-6 fatty acids, wherein the formulation further comprises:

a) a dosage of omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 or greater, wherein:

(i) omega-6 fatty acids are 4-75% by weight of total lipids and omega-3 fatty acids are 0.1-30% by weight of total lipids; or

(ii) dosage of omega-6 fatty acids is not more than 40 grams; or

b) polyunsaturated, monounsaturated, and saturated fatty acids, wherein the omega-6 fatty acids are greater than 20% by weight of the total lipids and nutrients comprising one or more polyphenols, or one or more phytochemicals selected from: phytosterols, organosulfides, melatonin, saponins, coumarins, lycopene, lutein, zeaxanthin, and monophenols.

Claim 14:
Use of one or more factors of a subject selected from: age of the subject, sex of the subject, diet of the subject, the body weight of the subject, physical activity level of the subject, lipid tolerance of the subject, medical conditions of the subject, family medical history of the subject, and ambient temperature range of the subject's living area as an indicator for selecting a lipid-containing formulation for administration to the subject,
wherein the formulation comprises one or more mutually complementing daily dosages of fatty acids comprising omega-6 and omega-3 fatty acids, wherein the ratio of omega-6 to omega-3 fatty acids and their amounts are based on the one or more factors; wherein the omega-6 to omega-3 ratio is:

4:1 or greater, wherein the dosage of omega-6 is not more than 40 grams; or
1:1 to 50:1 based on amount of antioxidants, phytochemicals, and seafood in the subject's diet and/or the formulation; or
wherein increase of omega-6 is gradual and/or withdrawal of omega-3 is gradual and the dosage of omega-6 is not more than 40 grams; or
wherein the fatty acid content is matched to Table 6.

The inventions were conceived because of the following reasons:

A. There is mass information and vilification of omega-6 in the prior art;
B. the inventor arrived at an insight into peculiar dose-effect of omega-6 fatty acids, finding health benefits at higher dosages of omega-6 than taught in the prior art combined with higher ratios of omega-6 to other lipids (other fatty acids, antioxidants, and phytochemicals);
C. dietary lipids are associated with health at fundamental level and incorrect lipid intake is associated with many diseases and medical conditions;
D. natural sources of lipids are unpredictable in lipid content;
E. less than 1% of the public understands lipids;
F. it is too complex for the public to prepare lipid dosages for different members of the family; and because
G. the innovations will set humanity on course to long-term solution to 100-year old lipid problem sparking downstream advancements in public health.

Prior art overwhelmingly teaches to reduce omega-6 and increase omega-3 intake, there is a widespread misconception in prior art that omega-6 is harmful to health[2], and dosage of omega-6 is poorly understood—stepwise increase in omega-6 was held to be harmful to health[3] whereas the Inventor finds beneficial effects at higher dosages of omega-6. Prior art overwhelmingly teaches omega-6 less than 1-3% of calories, and omega-6 to omega-3 ratio less than 3:1 and closer to 1:1 and even less than 1:1; prior art fails to teach dosage of total omega-6 fatty acids or teaches extremely low dosage of omega-6 such as 1g/day; and prior art fails to teach

[2] Simopoulos, Ann Nutr Metab 1999;43:127–130; Hamazaki et al. World Rev Nutr Diet. Basel, Karger, 2003:92:109–132; Lands, Ann. N.Y. Acad. Sci. 1055: 179–192 (2005)

[3] Ip et al., Cancer Research 45,1997-2001, May 1985; Lands, Nutrition Reviews 1986:44-6:189-95

formulations of omega-6 and domega-3 in consideration of total lipids (lipids include other fatty acids and lipid vitamins and lipid phytochemicals), typical teaching of omega-6 and omega-3 is in relation to total fatty acids or composition.

The scale of the problem is very large. According to WHO statistics, 33% of Europeans above the age of 15 have a chronic disease (e.g., heart disease, diabetes, cancer, asthma, ADHD), a large part of which is associated with mismanaged lipid consumption including omega-6 and omega-3 (also see Specification, publications[4], and declarations on record). Premature deaths of 550,000 working-age people across European Union countries from chronic diseases cost EU economies EUR 115 billion or 0.8% of GDP annually. This figure does not include the additional loss in terms of lower employment rates and productivity of people living with chronic health problems. (See http://www.oecd.org/health/europe-paying-a-heavy-price-for-chronic-diseases-finds-new-oecd-ec-report.htm).

For further details and evidence, see Attachment A, p. 4-6, Exhibit D, paragraphs [002]-[004], Exhibit E (Wikipedia pages one omega-6), and the case history on EP Register. Over 40 references are on record as evidence of above. Evidence submitted to EPO includes nine declarations from esteemed scientists, evidencing that there is mass confusion in the art (also evident from EPO citations) and that claimed inventions are extremely important for public health. For example, see Patents for Humanity application, Attachment A, Exhibit A, prepared for US Patent and Trademark Office for corresponding cases (e.g., US Patent 1029295 B2).

All the evidence demonstrates the misinformation is widespread and continues to date. **The misinformation is in part because piecemeal patents in the nutrition field create an environment in which misinformation flourishes and perpetuates.** For example, 100s of patents have been issued, each directed to a narrow application of low ratios of omega-6 to omega-3, which were then marketed with advertisements hyping omega-3 out of context.

Whereas the *unexpected* correct solution taught in the subject patent applications is higher ratio of omega-6 to omega-3 with restricted dosage of omega-6, *not* smothering omega-6 with omega-3, and consideration of other lipids in the formulation.

In other words, prior art failed to understand the unexpected synergistic effects of higher ratios of omega-6 to other lipids and the dosage of omega-6 and the direction in which to proceed. The Prior art as a whole taught reduced intake of omega-6 and sought to suppress its actions with other lipids because the near-term effect of increase in omega-6 produced adverse symptoms.

Therefore, the subject innovation solves a long-felt critical need in humanity and has immense and real potential to enhance and protect public health, but for such innovation to take hold a significant patent as claimed is necessary, which will allow clear teaching, facilitate partnerships for implementation of innovation, and eradicate misinformation.

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[4] E.g., Bhagat U. Das UN. "*Potential role of dietary lipids in the prophylaxis of some clinical conditions*" Arch Med Sci 2015; 11, 4: 807–818.

III. Improprieties in Examination And Appeal Review

A. EPO Rejected the Parent Case Under the Pretext of Article 123(2) Because EPO Could Not Reject the Claimed Inventions Under Articles 54 and/or 56 EPC

First, we discuss the premise of Articles 54 and 56, because inability to reject the claims under Articles 54 and 56 in the current case has led EPO to *overreach* and improperly apply other rejections such as "added matter" under Article 123(2) and Unity of Invention under Article 82 EPC. The real reason for the objections, evident from prosecution history, is to restrict the scope of the claims, which has compromised the innovation and will further compromise the innovation.

In 10 years of worldwide prosecution no prior art has surfaced that could legitimately be said to destroy the novelty of the subject claims in accordance with Article 54 EPC, and lack of inventive step objection in accordance with Article 56 EPC could not be legitimately maintained upon the claims due to new insights presented, disadvantages predicted in the prior art, unexpected results, continuing opposite teachings and misinformation in the art, and critical unmet public health need. (GL, G-VII, 9 and 10.1-3).

The legal requirements for novelty rejection under Article 54 EPC are very *strict* and rightly so. *In order to destroy novelty, the applicable prior art must disclose and enable the exact same invention with every single element as recited in the claims*. The underlying principle of novelty rejection is that public—skilled persons including competitors—has been fully informed of the exact solutions and how to practice them and there can be no doubt about this. There are a series of EPO case laws that have held:

1. Lack of novelty is a question of inevitability and not a question of probability (T12/81, T270/97, T583/01).

2. Subject-matter described in a document can only be regarded as having been made available to the public, and therefore as comprised in the state of the art pursuant to Art. 54(1), if the information given to the skilled person is sufficient to enable him, at the relevant date, to practice the technical teaching which is the subject of the disclosure, taking into account also the general knowledge at that time in the field to be expected of him (T 26/85, T 206/83 and T 491/99)(GL, G-VI, 4).

3. Disclosure can only be considered "implicit" if it is immediately apparent to the skilled person that nothing other than the alleged implicit feature forms part of the subject matter disclosed (T 95/97).

4. The teaching of a document, independent of its nature, is not to be interpreted as embracing equivalents not disclosed in that document (T 167/84, T 517/90, T 536/95).

"[w]hen considering novelty, it is not correct to interpret the teaching of a document as embracing well-known equivalents which are not disclosed in the document; this is a matter of obviousness" (GL, G-VI, 2).

5. A sub-range selected from a broader numerical range of the prior art is considered novel (see T 198/84 and T 279/89; and GL, G-VI, 8).

6. Generic disclosure does not take away the novelty of a specific disclosure (rivets are considered novel over generic fasteners) (GL, G-IV, 5).

7. Patenting is also not excluded where a dosage regime is the only feature claimed which is not comprised in the state of the art (G 2/08).

Thus, there is clear and ***purposeful*** distinction between lack of novelty and lack of inventive step, in that the law recognizes that in order to destroy novelty a prior art document must disclose and teach how to practice the ***exact same*** invention then only it can be said that this is in possession of the public. Furthermore, a selected range from a broader numerical range is considered novel.

For instance, if there were a reference that exactly described and enabled a formulation to cure common cold permanently, then common cold would be cured. It would defy every conceivable logic if there is a reference that exactly describes and enables the formulation to cure common cold (e.g., dosage of compound A above X g/day), yet billions of humans repeatedly suffer the misery of common cold. Therefore, it is flawless if a reference ***exactly*** describes and enables claimed limitations, then such claims are not novel.

However, if exact same formulation is ***not*** described in the prior art, it is ***not*** clear what aspect of the prior formulation is problematic (e.g., how much compound A in absolute and relative to compound B), and there are ***opposite teachings*** to the claimed formulation (e.g., dosage of compound A below X g/day) and the public continues to suffer from the misery (like common cold), then the claimed formulation (ratio of compound A to compound B Y:1 and compound A above X g/day) can neither lack novelty nor inventiveness.

However, ED-1 extremely improperly disregarded the ***principles built into the law*** in Articles 54 versus 56 EPC in examining the parent application. ED-1 improperly alleged that the subject claims are anticipated by individual oils, even though a mixture from different sources was inherent in the "formulation" claims presented to ED-1. Subsequently upon appeal Applicant explicitly recited "mixture of lipids from different sources" in the claims presented to BoA; to which BoA responded by alleging "added matter" in all claim requests including where ED-1 had conceded to no added matter, because BoA had no excuse left to sustain rejections under Article 54.

Thus, EPO rejected all claim requests under the pretext of "added matter" under Article 123(2) EPC because rejections under Articles 54 and/or 56 EPC could not be sustained.

(i). ED-1 Conceded That Article 123(2) EPC was Satisfied in AR9-10 but Applied Article 56-type Rejections Under the Heading of Article 54 EPC to AR9-10

ED-1 applied improper "added matter" objections under Article 123(2) EPC to Main Request and Auxiliary Requests 1-8 but conceded there was no added matter in Auxiliary Requests 9 and 10[5] ("AR9" and "AR10"), to which it applied improper "novelty" objection under Article 54 EPC.

Despite strict anticipation requirements (and evidence of public suffering) ED-1 rejected the parent application, AR9 and AR10, over alleged anticipation by each, D7 (reconstructing example 5 in hind sight) and D10 (fatty acid content of individual oils, alleged for the first time at the Oral Proceedings[6]), disregarding the terms "formulation", "dosage of omega-6 and omega-3", and "by weight of total lipids" recited in Claim 1, but neither recited nor enabled in D7 or D10[7]. Alleged anticipation by both D7 and D10 by ED-1 is astoundingly improper. Further, AR10 was *solely* rejected over alleged anticipation by mere recital of fatty acids in each of soybean oil, walnut oil, and wheat germ oils, in a table in D10 (see cited table below) and other phytochemicals possibly present in such oils based on food composition tables (D16).

EFA PARENT OMEGA 6 AND PARENT OMEGA 3 COMPOSITIONS OF SEEDS

		fatty acid percentage in oil						
Seeds		Polyunsaturated			Monounsaturated	Saturated		
Name	Fat Content in seed (%)	LNA 18:3w3 (%)	LA 18:2w6 (%)	LNA+LA w3+w6 (%)	18:1w9 (%)	18:0 (%)	16:0 (%)	Total (%)
hemp	35	20	60*	80	12	2	6	8
chia	30	30	40	70	-	-	-	-
kukui	30	29	40	69	-	-	-	-
flax	35	58	14	72	19	4	5	9
pumpkin	46.7	0-15	42-57	57	34	0	9	9
soybean	17.7	7	50	57	26	6	9	15
walnut	60	5	51	56	28	5	11	16
Wheat germ	10.9	5	50	55	25	18	0	18
evening primrose	17	-	81**	81	11	2	6	8

[5] Decision March 3, 2015, p. 14-15.
[6] Copying improprieties of the USPTO, see enclosed Letter to the Congress of the United States, Attachment J.
[7] Decision March 3, 2015, p. 14-16.

As noted above in Section II, at least dosage of omega-6 and relevance of omega-6 to total lipids is not well understood in the art. Then how did ED-1 decide that the ***skeletal*** disclosure of the composition of individual oils describes and enables the subject "formulation" claims drawn to "dosage" of omega-6 and omega-3 and their concentrations in relation to "total lipids", which tables are in public domain, but popular media, international scientists, various governments, and industry overwhelmingly teach to mix these oils to achieve low absolute and relative intake of omega-6 fatty acids[8]? *In other words, the individual oils in the prior art have neither disclosed the lipid dosages, the focus of the present invention, nor enabled the solutions to public suffering.*

Specificity **in patent law has always been held as not anticipated by general prior art disclosure, and** ***neither the EPO nor the courts*** **have had any difficulty in examining and upholding** ***specific disclosure and enablement*** **as not anticipated by general prior art**, as noted above in Section III.A, points 1-7. Neither would an individual oil composition enable a skilled person to inevitably practice omega-6 dosages as taught in the subject disclosure (T12/81, T270/97, T583/01) based on state of the art at the time of the disclosure (T 26/85, T 206/83 and T 491/99), nor would it be immediately apparent to skilled person to practice the dosages as taught and consider omega-6 concentration in relation to total lipids from individual oils (T 95/97), nor is it proper to interpret equivalents not disclosed in the document (D10), that is a matter of obviousness (T 167/84, T 517/90, T 536/95). Furthermore, as evident from Attachment A, Exhibit D, paragraphs [002]-[004] and Exhibit E, there is still debate in the art on the claimed subject matter. Therefore, at least lack of enablement by D7 and D10 and that D10's individual oil is not even a "formulation" was a dispositive point to ruling non-anticipation by D7 and D10, which ED-1 failed to do.

ED-1 applied "novelty" objection under Article 54 EPC because "lack of inventiveness" objection under Article 56 EPC could not be sustained because of opposite teachings, and long-felt critical unmet need. **Thus, ED-1 threw out the public interests, the very purpose why there is a distinction between lack of novelty and lack of inventiveness, and** ***unilaterally*** **decided that public suffering was unimportant and** ***overruled*** **the EPC** (see discussion above in Section III.A).

Many of the additional objections ED-1 raised are also so far-fetched that they make EPO unworthy of respect. Such as alleging lack of clarity in "age of the subject"[9] which appears in 100s of dietary guidelines in every country, or alleging that fatty acid profiles of tissue samples in experiments in cited references anticipate the claimed formulations for ingestion[10], or alleging lack of unity in a perfectly unified claim set.

Only the most egregious aspects are presented here to not overwhelm the delegates with detail. However, further details can be seen in Attachment A (e.g., pages 6-10) and at EPO Register.

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[8] Ip et al., Cancer Research 45,1997-2001, May 1985; Lands WEM Nutrition Reviews Vol 44. NO 6. June 1986; Simopoulos et al., Ann Nutr Metab 1999;43:127–130; Lands WEM. Ann. N.Y. Acad. Sci. 1055: 179–192 (2005)
[9] Decision March 3, 2015, p. 5.
[10] Summary of call with Chairman submitted to EPO on February 3, 2015, p. 2 #3.3.

(ii). BoA Applied Article 123(2) EPC Rejections to <u>ALL</u> Claim Requests Even Where ED-1 Skilled Persons Conceded Article 123(2) Was Satisfied
<u>AND</u>
BoA Colluded with Applicant's Own Representative to Undermine the Applicant

In order to overcome the ED-1 improper anticipation rejections over individual oils, the claims presented to BoA were amended to recite,

"A lipid-containing formulation comprising a mixture of lipids from different sources…"

Additionally, despite disagreeing with all objections Applicant made good faith serious efforts to overcome all objections, submitting on 09 July 2015, 21 alternate claim requests (Main Request and 20 Auxiliary Requests) successively overcoming <u>all</u> Articles 123(2), 82, 84, 54 and 56 EPC objections with 63-page Grounds of Appeal thoroughly rebutting the objections.

Two years later, on 18 April 2017 BoA issued a communication reraising some points rebutted in the Grounds of Appeal, without a word about the rebuttals. This was shocking because then what is the point of submitting Grounds of Appeal? Even if additional grounds were raised, counter argument should have been given to the rebuttals or the objections that have been rebutted should have been withdrawn. For detailed discussion see Attachment A, p. 17-21.

Nonetheless, Applicant responded to BoA communication on 28 June 2017 in a conciliatory tone with arguments and two additional Auxiliary Requests. However, BoA disregarded these arguments also, as discussed below. Again, then what is the point of submitting a response to BoA communications?

At the oral proceedings held in July 2017, BoA stated at the outset that it was minded of rejecting the application because of "*<u>possible</u>" in other words, *<u>perceived</u>* anticipation by prior art. See Attachments A p. 25-26 and B p. 2. **In other words, *<u>only for this case</u>*, BoA had overruled the law discussed above in Section III.A that to be anticipatory the prior art must inform public—skilled persons including competitors—of the exact solutions and how to practice them *<u>with specificity and without ambiguity</u>*** and disregarded overwhelming evidence that a competitor could not obtain the claimed subject matter because competitors were teaching and claiming the opposite subject matter even after the filing of the subject application. See Grounds of Appeal submitted on 09 July 2015, p. 32-61; also see US Patent 7759507 issued on 20 July 2010 claiming, "the ratio of said omega-6 fatty acids to said alpha-linolenic acid (C18:3n-3) [one of the omega-3 fatty acids] is from about 0.25:1 to about 3:1"; and Attachment A Exhibit E accessed on 29 January 2018.

Because no legitimate anticipatory prior art could be cited BoA applied the allegation of "added matter" under Article 123(2) EPC to <u>ALL</u> the claim requests.

BoA zeroed in on the *combination* of features recited below alleging "added matter" because the combination was recited in Claim 1 of all claim requests; in this way BoA could reject all requests in one stroke.

> "a dosage of omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1…"
> and
> "omega-6 fatty acids are 4-75% by weight of total lipids and omega-3 fatty acids are 0.1-30% by weight of total lipids."

This was improper because:

a) Applicant had already rebutted this objection in the response to BoA communication (points 7.3.1-7.3.5) submitted on 28 June 2017, asserting Tables 14-19 and original Claim 8 explicitly teach that formulations comprising ratios of omega-6 to omega-3 fatty acids are combined with their concentrations in reference to total lipids; and even if it was not explicitly taught it is permissible to combine separate items belonging to different embodiments described in one and the same document, if such combination has specifically been suggested (see T 305/87), which is suggested in Example 1 for instance.
b) ED-1 had not objected to the *combination* in any of the requests. AR9-10 submitted to ED-1 reciting this combination were not held to "add matter" by ED-1. ED-2 has also not objected to the combination in the divisional case (Written Opinion March 14, 2018, p. 21) (though ED-2 is otherwise improper, see Section III.C below). Examiners are skilled persons, evidencing claimed *combination* is easily obtainable by skilled persons.
c) Applicant had provided declarations from five different scientists (Pan and Shen declarations submitted on 9 May 2014, and Erickson, Rustagi, and Rucker declarations submitted on 5 December 2014) that the claimed subject matter is directly and unambiguously obtained from the Specification.

Additionally, BoA improperly alleged that omega-9 fatty acids were an essential feature of the claimed subject matter. It should be noted that omega-9 fatty acids are *not* recited in original claim 1.

For further detail see Attachment A, p. 19-21, 25-26, 27-28 and response submitted to BoA communication on 28 June 2017, p. 12-15.

Most disturbingly, BoA colluded with applicant's own representative to undermine the applicant.

The representative, Mr. Michael Alt initiated the behavior by objecting to the Applicant's CEO, Ms. Urvashi Bhagat (the undersigned) from arguing at the oral proceedings and repeatedly obstructing Ms. Bhagat. Although at first instance BoA said that there was no issue with the Ms. Bhagat making the arguments because the proceedings were ex-parte, but subsequently by laughing at such occurrences, BoA encouraged Mr. Alt and undermined the Applicant.

The Board's minutes do not record this pivotal occurrence. Therefore, it is very important that there should be exact account of all BoA hearings, independent from the Board's minutes.

Applicant requested on 20 December 2017, that page 2 of minutes be corrected as follows to reflect this occurrence.

> "Ms. Bhagat attempted to make arguments before the Board when Mr. Alt interrupted her. Chairman said that there was no issue with Ms. Bhagat making the arguments, because the proceedings were ex-parte. However, when Ms. Bhagat attempted to speak again, Mr. Alt threw his pen making it uncomfortable for Ms. Bhagat to speak subsequently. The Board laughed at the lack of support from the counsel." See Attachment B, p. 2.

Detailed account of this behaviour is described in Attachment A, p. 23-26; and evidenced in Exhibit C, Applicant's Correspondence with Mr. Alt of Bird and Bird, 16 August 2017 to 18 September 2017, and Exhibit D.

Ms. Bhagat testified in Exhibit D paragraphs [0012]-[0015) of this humiliating experience. Specifically, see following testimony in paragraph [0014]-[0015]:

> *"From this point on the discussion in oral proceedings deteriorated. Mr. Alt was making feeble arguments, not citing what I wanted him to cite, and obstructing me from speaking, and the Board was an accomplice. There was an apparent collusion between Mr. Alt and the Board to undermine the subject application.*
> *Although I sporadically tried to argue again during the rest of oral proceedings, it was difficult for me to do so, because of objections and lackluster support from Mr. Alt, and the undercurrent of collusion among the Board and Mr. Alt. Each time I spoke, I spoke worriedly and hurriedly to avoid being cut off and the Board ridiculing and subverting the arguments."*

Furthermore, BoA dispatched the Minutes of Oral Proceedings on 03 August 2017 stating,

> "[t]he Chairman gave the Board's conclusion that claim 1 [of Main Request] did not meet the requirements of Article 123(2) EPC." (Bottom of page 2).
> "[t]he Chairman gave the Board's conclusion that claim 1 of none of Auxiliary Requests 1 to 22 complied with Article 123(2) EPC." (Bottom of page 3).

Applicant objected to "the Board's conclusion" and requested that the minutes be corrected because the appeal was withdrawn when the BoA Chairman had said, "I have only given Board's preliminary views, not conclusions." See Exhibit D, paragraph [0020] and Attachment B, p. 2-3.

BoA refused to correct the minutes on 17 January 2018, denying the incidences obstructing Ms. Bhagat from presenting Applicant's case at the oral proceedings and insisting "the Chairman did explicitly give conclusions (not just preliminary views) on the allowability of the main request and the auxiliary requests 1 to 22 under Article 123(2) EPC. See Attachments B and C.

If BoA did give "conclusions" and insisted that those were not "not just preliminary views", then why did BoA allow withdrawal of the appeal? The only logical explanation is that BoA wanted its minutes to be treated as "decision" in examination of the divisional application, without having to affect the case law, singling out the subject case for maltreatment[11].

This is injustice! BoA and the representative made mockery out of the oral proceedings compromising the credibility of the legal profession and EPO.

[11] Applicant and its later legal representatives have searched the EPO database for minutes of oral proceedings where the appeal was withdrawn and such minutes recite any "conclusions" given at the oral proceedings, no such case was found.

B. The Enlarged Board Turned a Blind Eye to Evidence of Malfeasance in Its Review

Applicant filed a Petition for Review by Enlarged Board of Appeal under Article 112a EPC on 26 March 2018, in view of the following:

- Violation of right to be heard, since Applicant was obstructed from submitting its case at the Oral Proceedings held on 27 July 2017;
- BoA's refusal to correct the minutes on 17 January 2018, insisting that it gave "conclusions (not just preliminary views)" synonymous with "decision"; and
- The adverse effect on Applicant's divisional application, i.e., ED-2 treated BoA's minutes as a "Decision"—Written Opinion issued in the Divisional case on March 14, 2018, p. 2., states, "the earlier (Parent) application has been refused for deficiencies under Article 123(2) EPC." (As noted in Section III.A(i) above, ED-1 refused the parent application (AR9-10) for alleged deficiencies under Article 54 EPC, not Article 123(2) EPC. Thus, ED-2 treated BoA's "minutes" as a "Decision" and gave similar objections as BoA.)

Applicant asserted that in accordance with Article 112a (2) lit. (c), (d), and (e) EPC the Petition is based on the grounds that,

> (c) a fundamental violation of Article 113 occurred in that Petitioner's right to be heard was violated;
>
> (d) a fundamental procedural defect defined in the Implementing Regulations Rule 142 and Article 133(2) occurred in the oral proceedings held on 27 July 2017 in that the Petitioner was unrepresented (as noted in Section III.A(ii) Mr. Alt in effect represented the BoA not the Applicant); and
>
> (e) a criminal act established under the conditions laid down in the Implementing Regulations had an impact on the oral proceedings and the "conclusions" imposed by the Board, in that there was a collusion between the Board and Mr. Michael Alt of Bird and Bird (Representative 1), at the oral proceedings held on 27 July 2017, to undermine the Petitioner.

Among evidence, Applicant submitted Exhibit C, Applicant's Correspondence with Mr. Michael Alt of Bird and Bird, 16 August 2017 to 18 September 2017, and Exhibit D, Declaration of Ms. Urvashi Bhagat dated January 30, 2018. For example, Mr. Alt admitted that he obstructed Ms. Bhagat from speaking, stating, "I… aimed at controlling your submission" (see Ms. Bhagat's email of 16 August 2017 and Mr. Alt's response of 31 August 2017).

Among relief, Applicant requested that the oral proceedings of 27 July 2017 be invalidated, and the appeal proceedings be reopened.

For further details, see Attachment D, Petition for Review by the Enlarged Board of Appeal under Article 112(a) EPC submitted on 26 March 2018.

The Enlarged Board of Appeal (EBoA) issued a communication on 12 June 2018. **Applicant was surprised to find that EBoA too had acted improperly *disregarding the evidence cited in and submitted with the Petition***.

In its response to EBoA communication on 22 July 2018 (see Attachment F) Applicant pointed out the following:

(i) EBoA had *not acknowledged key evidence* Exhibit C and Exhibit D submitted with the Petition, and Applicant corrected EBoA's enumeration of "Facts."
(ii) BoA minutes were a "Decision" because of
    a. the *substance* of the contents e.g., "conclusions" (synonymous with "decision") versus "preliminary views" in the paper titled "Minutes of the oral proceedings" and the BoA itself had insisted in its refusal (Attachment C) that the "conclusions" are "not just preliminary views",
    b. the *finality* of the "minutes" on the case,
    c. BoA made *reasoned choices* in arriving at "conclusions",
    d. the *procedural context*, where Representative 1 was in collusion with BoA, and
    e. that *EPO itself had held the minutes to be decision* in the divisional case.
(iii) Applicant's *right to be heard was violated* because Applicant was obstructed in submitting its case.
(iv) There was *criminality in the act* where Representative 1 was in collusion with BoA.
(v) The withdrawal of the appeal was *induced by BoA.*

Applicant also asserted that the objections could only be raised when the Board refused to correct the minutes on 17 January 2018 to state "preliminary views" instead of "conclusion" (synonymous with "decision") and when BoA confirmed that it was in collusion with Representative 1 by declining to correct the minutes (see Attachment C).

See Attachment F for detailed response.

On 10 October 2018, EBoA issued its Decision *again* disregarding glaring evidence repeatedly called to attention. Annotated copy of the Decision R4/18 of the Enlarged Board of Appeal of 10 October 2018 is attached here as Attachment G.

Additionally, Applicant made of record the reasons why EBoA decision was improper in a Formal Complaint submitted on 12 November 2018 (Attachment H), where the Applicant's contentions included the following:

1. EBoA has disregarded evidence Exhibits C and D repeatedly cited in the Petition (see page 5 (points 7.a, 7.d), page 6 (points 7.f-g), page 7 (points 7.h-i), and page 8 (points 7.k and 9)), and throughout in the response to EBoA communication. The statements of employees of one of the parties were regarded as sufficient evidence in a series of appeal cases, e.g. T 162/87 and T 627/88, T 124/88, T 482/89 (OJ 1992, 646), T 363/90, T 830/90 (OJ 1994, 713), T 838/92 and T 327/91, T 190/05, J 10/04. Accordingly, EBoA should have honorably considered the Exhibit C and D.

2. What other evidence does the EBoA expect? Only five people were present in the oral proceedings. Four of them (Representative 1 and BoA) were in collusion against the Petitioner. Partners in crime do not implicate other partners. The fifth, the Applicant's

CEO gave testimony, Exhibit D, supported with Exhibit C. Besides the Applicant's CEO, does EBoA expect the walls to testify? It is noted that EPO ensures that there is no evidence of its wrongdoings at the oral proceedings by generally not allowing any cameras and sound recordings[12].

3. When the BoA expressly stated in its refusal to correct the minutes "the Chairman did explicitly give conclusions (not just preliminary views) on the allowability of the main request and auxiliary requests 1 to 22 under Article 123(2) EPC," (emphasis added) it confirmed that "conclusion" is different from "preliminary views". BoA made it clear that it did not use "views" or "conclusions" as alternates, or synonyms. In other words, BoA insisted that it gave a "decision." Further, in the submission of 22 July 2018 (pp. 11) it was evidenced "conclusion" and "decision" are synonyms in the English language. EPO cannot distort the language per its convenience.

4. BoA wanted its minutes to be treated as a "decision" without having to formally issue a decision, that is why it insisted it gave "conclusions" and therein lays a major wrongdoing.

C. ED-2 in the Divisional Case Takes License for More Improprieties from BoA and EBoA Improprieties in the Parent Case

As called to attention in Section III.B above ED-2 treated BoA "minutes" as a decision, and took license for improprieties from BoA as evidenced by the following:

a) ED-2 explicitly stated in the Written Opinion issued on March 14, 2018, p. 2., "the earlier (Parent) application has been refused for deficiencies under Article 123(2) EPC." However, as noted in Section III.A(i) above, ED-1 refused the parent application (AR9-10) for alleged deficiencies under Article 54 EPC, not Article 123(2) EPC. Thus, ED-2 treated BoA's "minutes" as a "Decision".
b) ED-2 took cues from BoA. For example, ED-2 alleges that omega-9 fatty acids are an essential feature of the invention in Written Opinion issued on March 14, 2018, p. 3-4, #1.2, similar to BoA allegation (Attachment B p.2.), but ED-1 skilled persons could obtain from the disclosure that omega-9 fatty acids are not an essential feature and held AR9-10 (which do not recite omega-9 fatty acids in claim 1) to comply with Article 123(2) EPC.

Further, when EBoA condoned BoA improprieties, then it was clear to ED-2 that they were free to disregard the law and evidence because the entire chain of command at EPO will condone their malfeasance.

Furthermore, taking their cues from BoA and EBoA ED-2 goes a step further in improprieties, and alleges that the recitation in claim 1 in terms of "by weight of total lipids" *also* "adds matter" and therefore violates Article 123 (2)/76(1) EPC (see Written Opinion p. 1.2.1), which neither ED-1 nor BoA had alleged.

[12] GL E-III, 8.2.1 and 10.1; and Notice of the Vice-Presidents Directorates-General 2 and 3 dated 25 February 1986, OJ EPO 1986, 63

It should be noted that original claim 1 does not recite omega-9 fatty acids, and the terms "by weight of total lipids" are the preferred embodiments throughout the original disclosure, e.g., claims 35, 36, and 38.

For detailed arguments, see responses of 02 November 2018 and 25 June 2019 (Attachment I) thoroughly rebutting all objections raised in the Written Opinion and Exam report dispatched on 25 February 2019.

Therefore, Applicant is justified in being filled with indignation from the poor treatment it has received for the last 10 years from EPO, especially for such an important invention for public health, which EPO should have advanced out of turn and allowed quickly.

IV. EPO Has Disregarded Numerous Complaints Submitted and Issues Brought Up by the Applicant

Applicant has submitted numerous complaints to EPO in the Parent and Divisional cases including the ones listed below. Almost all of which were addressed to Mr. Piotr Wierzejewski, Administrator Quality Management, the President, Secretary of the Administrative Council, Karin Seegert (Chief Operating Officer Healthcare, Biotechnology & Chemistry), Titia Kanbier (Examiner of the Divisional Application), and Reinoud Hesper (Patent Law). Some of the complaints were also addressed to EBoA. The appeals to BoA and EBoA are also technically complaints, but they are not listed below, as they have been separately addressed above.

1. 25 September 2017 Email – Issues brought up: Substantially similar claims were submitted to dozens of other jurisdictions, which do not find "added matter." Is EP skilled person particularly inept? (There is no difference in scientific training in European countries and other countries, neighboring Israel, for example. Then why does EPO allege "added matter" as a rule, rather than exception as in other jurisdictions? Intellectual Property High Court of Japan and Intellectual Property Trial and Appeal Board of South Korea overturned the respective patent office's lack of support, clarity, and enablement objections in the corresponding Applications. See the respective translated decisions with the claims in Attachments K and L.)

2. 11 December 2017 Email – Issues brought up: Same as above and that mindlessly restricted patents are harming the health of millions of Europeans and obstructing innovations.

3. 30 January 2018 Formal Complaint — See discussion under Section III.A above and Attachment A with Exhibits A-E.

4. 12 February 2018 Email – Issues brought up: Response to Mr. Wierzejewski's letter of 01-02-2018. ED-1 and BoA raised clarity objections on everyday terms and "added matter"

objection on matters that are easily derived by dozens of patents offices around the world, and that there were divergent holdings by ED-1 versus BoA. Then they are just raising objections as convenient, without justification. We understand that EPO is obliged to observe EPC together with Guidelines for Examination, as well as jurisprudence of the Boards of Appeals, but that is exactly the problem, that they were ***not*** observed by ED-1 and BoA as detailed in the Formal Complaint dated 30-01-2018. Further, you have also alluded that Patent Prosecution Highway is a hoax by saying that allowance at JPO has no bearing at EPO.

5. 26 February 2018 Email – Issues brought up: The manner in which EPO insists that applicants work through lawyers, combined with the manner in which EPO controls the lawyers practicing at EPO, essentially equates EPO exploiting small inventors in collusion with lawyers. See details with evidence in our Formal Complaint dated January 30, 2018. Lawyers are worried about their relationship with EPO, EPO is concerned about fees that it collects (EPO is one of the few jurisdictions that requires annuity payments before patent grant, and the highest annuity fees), and EPO is the most unreasonable in that EPO denies restatements as "added matter." Then EPO is an unethical revenue focused business that induces disclosure and denies rights, heedless to innovation. There were five people in the room at the oral proceedings held on 27 July 2017. The Board (three men) with an agenda to deny patent because it would have solved many problems (unfavorable to EPO revenue), the lawyer (one man) concerned about maintaining his relationship with EPO/Board and uninterested in solving the problem because that might adversely affect his revenue streams from other clients. The inventor/applicant was alone, ganged upon, and violated. We hope EPO can understand why we are so upset. There should be impartial public representatives present at oral proceedings; minutes to oral proceedings should be taken by a public body via audio recording; self-representation should be made easier; and oral proceedings should not be held in cases where applicant is outnumbered, in favor of written communications.

6. 20 March 2018 (three Emails) — Issues brought up: ESR issued by EPO in the divisional case on March 14, 2018, alleged added matter mindlessly. If EPO thinks skilled persons, for example, MD/PhDs in this case, are so dumb, then EPO's existence is futile. There is no justification for existence of an organization whose charter on one hand is innovation but on the other hand is so rigid that it suffocates innovation. Added matter has to be considered in context of the invention and disclosure. In this regard, every single person everyday consumes n-6 and n-3 through their diet. After reading our disclosure a biology major (a skilled person) can understand the invention and derive the claimed subject matter without any difficulty whatsoever. It is a separate matter that they likely won't be able to practice the disclosure in daily life, because lipids are unpredictable in their sources. That's why commercial structure that we are building is necessary.

   Why don't the examiners honor that literal support is not required?

   Why don't the Examiner's honor that support is similar to novelty question?

Everything we have claimed is not novel for subsequent filers. (see T 667/08, T 201/83, T 305/87, and T 190/99).

Moreover, the EPO applies different standards when reading the Applicant's disclosure, in that it alleges nothing is disclosed, but when reading prior art, it conveniently adds on to prior art to allege anticipation or obviousness.

Purpose of the emails is not to give arguments. We will properly respond to the substantive EPO examination reports through our EPA attorney. The point in these emails is to call attention to the improprieties and double standards at the EPO. EPO is willing to do anything to knock down inventions. We want to ensure that top management is aware of how EPO is abusing inventors. You are making public ill and you are abusing inventors, contrary to the interest of the public. This is crime. Plain and simple!

7. 21 March 2018 (two Emails) — Issues brought up: The the last few emails were written because the written opinion of 14.03.2018 is highly improper. When alleging "added matter" EPO is rigid, basically negating almost all of the disclosure, but when alleging anticipation and obviousness, EPO embellishes the prior art extensively. That is our objection. The alleged "added matter" comes from minds unwilling to understand. We have seen "allowable subject matter" at page 21 of the written opinion. **The issue is that the EPO is changing the essence of the invention**. If you limit us the way you are, then we can't effectively solve the problem. There is a lot of noise in this art. We have to overcome that, and we can do that by clear teaching and building collaborations. It takes several decades and resources to solve this kind of problem. **You have already reduced us to 10-year patent term and now you are compromising what we can do with that. This is the reason for our anguish**.

8. 09 October 2018 Email — Issues brought up: Response to the Written Opinion issued in divisional case on 14.03.2018 is submitted. The support table that was submitted with the claims was ignored. Such thoughtless objections were raised, that it is simply not possible to stay calm after almost 10 years of prosecution. The objections have been applied with eyes closed to the EPO Guidelines for Examination and case law. We are having to submit long arguments again, and again, and again. So far, we have submitted ***fifteen*** papers in the parent and divisional case and numerous evidence documents. This is a total abuse of process and obstruction of innovation, contrary to EPO charge. The purpose of examination is to earnestly ensure disclosure, clarity, enablement, novelty, and invention. It is not to delay, drag, and compromise innovation by making excuses and misapplying the law. It is clear from our experience with EPO that EPO uses "added matter" as an excuse to compromise innovations and inventors. For example, what part of "Literal support is not required" (see T 201/83, G 0001/93, T 667/08, G 0002/10, GL H-IV, 2.2) do the EPO personnel not understand? You must understand not all problems can be solved by mere disclosures. So just because we have disclosed it does not mean that public

has derived the full potential benefits of the innovation. For some problems to be solved a protected environment is necessary to nurture and implement the innovation. The current innovation such, which without adequate patent protection is extremely difficult to implement above the noise in the art.

9. 22 October 2018 Email to EBoA — Issues brought up: The decision R 04/18 is extremely improper. Applicant's testimony (Attachment A, Exhibit D) was ignored, which testified that Board was improper in laughing in concert with Mr. Alt (highly inappropriate) and made a mockery of the oral proceedings. Conduct at the oral proceedings is important as per EPO case law. If this is how EPO and those who are authorised to represent different clients before the EPO such as EPAs, behave at oral proceedings, then it is clear why attendance at oral proceedings has been dropping. It is beyond doubt that the EPO has created a system, where EPO in collaboration with the lawyers exploits inventors and sabotages innovation. EPO has set up ways of denying patents, prolonging prosecution, while increasing revenues (fees) to EPO. EPO chop off arms and legs of innovation, under pretext of "added matter" so meaningful advancement does not take place.

10. 12 November 2018 Formal Complaint Upon Enlarged Board — See discussion under Section III.B above and Attachment H.

11. 25 November 2018 Email — Issues brought up: Treatment of the subject applications is violation of human rights and obstruction of sustainable development. Applicant is inclined to file a complaint at the United Nations, the ECJ and ECHR, because,

    a. Patent practice is skewing the marketplace in favour of drugs and devices.
    b. When nutrition patents are granted, they are severely restricted which causes confusion and makes the problem worse, as EPO is doing under the pretext of "added matter" and "unity of invention".
    c. Public has been paying for lipid patents since 1870s (https://en.wikipedia.org/wiki/Margarine) but the problem has not gone away.
    d. The very issue is that they are not formulating lipid dosages by demographics, which is the necessary foundation, but they are inventing different oil mixtures, or structurally altering molecules.
    e. It was a German patent of structurally altered fats (https://en.wikipedia.org/wiki/Wilhelm_Normann) that gave us hydrogenated fats and caused worldwide diseases for 100 years.
    f. Thus, occasionally, some mixtures/molecules are promoted but then they realize it does not solve the problem or causes more problems and come back to square one. The result is lipid delivery to public has not substantially advanced in 6000 years.

    Because lipids are associated with health at a fundamental level, and nature is unpredictable in lipid content, public suffers at a mass scale. It is a particular problem for impoverished populations. (Patents for Humanity application, Attachment A, Exhibit A was enclosed.) The lipid problem will not go away unless solved as we have proposed and

that is a massive undertaking requiring funds for implementing and teaching, and to be able fend off those who will try to undermine our efforts. The EPO has already compromised and sabotaged the innovation with 10 years of delay.

12. 03 December 2018 Email — Issues brought up: The European lawyers and the EPO collude to compromise innovation because lawyers and EPO find it lucrative to issue many restricted patents at the expense of innovation. This is why there is no material progress in many arts.

13. 11 March 2019 Two Emails — Issues brought up: Exam Report of 25 February 2019 is improper as evidenced by the following:

    a. Written Opinion dated 14.03.18, cf Form 1507, sheet 24, #14.1; also communication dated February 25, 2019, sheet 6: Under what shameful logic did the Examiner allege that Claim 1 of D1 teaches O**6** to O**3** ratio of 5:1 to 10:1. The correct disclosure in D1 is "a lipid source having an omega **3** to **6** fatty acid ratio of approximately 5:1 to about 10:1." (See Claim 1 and Summary of Invention).
    b. All the arguments that were submitted in supplemental response in November 2018 were ignored.
    c. Table of support filed in October 2018 was ignored. We are the inventors, we know the Specification inside out, but it is the insistence of Examiners that they will construe the Specification in a way that allows them to compromise innovation.
    d. Table of Support submitted with claim filing in October 2017 was ignored.
    e. Examination Guidelines were ignored.

    As evidenced by the above, EPO makes disclosure up or it negates disclosure as convenient. Reader at EPO doesn't understand because the reader is **not** inclined to understand. ED-2 can't even obtain from the disclosure what ED-1 in parent case could.

    Patents are **not** charity. We did not ask for some "allowable subject matter." We set out to solve the problem. EPO is compromising the innovation and public health by improperly restricting us. It is unacceptable. It is no wonder that patents accomplish nothing, and public continues to suffer. In 100 years, the lipid problem has not been solved. It is because of such improprieties. EPO is focused on revenue from many small patents not on solving problems.

14. 13 March 2019 Email — Issues brought up: The purpose behind emailing EPO with copies to the President and Council Secretary is that EPO has abused the process for so long that at this time it is necessary for us to give it back unvarnished in plain words that EPO is committing crimes against inventors and public at large. We want this to be noticed in real time by the President and Council Secretary. Therefore, we email whenever we notice something atrocious. **Extraordinary measures are necessary because EPO has refused to give us just examination in past nine years**. Improprieties in discussions on 12 March 2019 with current representative Dr. Radkov were listed and it was said that formal substantial arguments will be submitted by Dr. Radkov. Such

extreme improper examination should never happen in the first place. Purpose of examination is to ensure that public is not already in possession of the claimed subject matter. It is not to harass applicants knowingly and compromise innovation. **EPO is aware that the objections applied are improper, but EPO does that anyway to restrict applicants**. EPO has not understood let alone fully appreciated that EPO through its actions is obstructing innovation and causing harm to the public at large. At this rate we could be 100s of years further and the lipid problem will never be solved, rather more mess would have been created from issuing many restricted patents (and patents like hydrogenated fats). **We hope to wake up seniors at EPO through these emails, as to the wrongs currently going on at EPO**.

15. 14 March 2019 Email — Issues brought up: In-part we are having so much difficulty with the case is that ridiculously improper Unity of Invention objections were applied in the parent case. In order to overcome the improper Unity of Invention objections we had to change the structure of the claims, which is still within our rights, but not the ideal way of writing the claims. Better way of writing the Claim 1 is as in the Main Request submitted in the parent case to ED-1 and the BoA. We will formally address this in due course in the divisional case. In the meantime, we request the responsible people on this list to counsel the Examiners not to apply improper Unity of Invention objection. Then claims can be written as they should be.

16. 27 March 2019 Email — Issues brought up: Additional contentions (in the divisional case), for the review and action of EPO personnel on the list after further review of exam report dated February 25, 2019 and the results of March 12, 2019 EPO consultation with Dr. Radkov mailed by EPO on March 20, 2019. **EPO demonstrates contempt for inventors and their time and financial means, innovations, and public at large by ignoring arguments and evidence submitted over and over and over again—over last nine years in these cases.** For example, on November 2, 2018, we submitted a 27-page long response rebutting each and every of points and sub-points 1-13 in the written opinion dated March 14, 2018, which the Examiner has entirely ignored. Examination Guidelines (GL) are a sham and by extension EPO is a sham, if the Examiners can ignore the Guidelines. For example, the Examiner has ignored the following in examination: GL H-IV, 2.2 (literal support is not required), 2.4 (a combination of the preferred disclosed narrower range and one of the part ranges lying within the disclosed overall range on either side of the narrower range may be derivable from the original disclosure), Article 69(1) EPC (claims determine the scope of disclosure), and G-VII, 5.4 (each feature has to be evaluated in examining novelty and inventiveness). It is clear from the communications that the quality of product in question does not meet the standards set by the President of the EPO. Accordingly, we also consider Director Quality Management's letters to us dated February 9, 2018 and November 22, 2018, to be improper because examination is **not** in accordance with the Guidelines or standards set by the President of the EPO. “Practice of the EPO” (raised in exam report dated Feb 25, 2019, p2) is ultra vires created by EPO Examiners. This has no place in patent examination. Either something is within the law or it is not. There is

no such thing as "this is our practice", which implies "Yes, we know it is contrary to the law, but we can choose to do so." That is absurd. It cannot be tolerated in the 21st century.

17. 28 March 2019 Email — Issues brought up in response to Mr. Wierzejewski's email of 28 March 2019: So far EPO has failed to properly read and respond to over a dozen responses and complaints submitted in the parent and divisional cases, not to mention 20-40 evidence documents that have been submitted evidencing opposite teachings and long-felt critical unmet public health need. EPO is astoundingly improper, such that it cannot even read a plain and simple table—Table 20, listing ~80 nutrients and 40 lipids and their dosage ranges and three paragraphs above the table. You note Guidelines, GL E-VI, 4, but you conveniently ignore the other parts of the Guidelines, such as GL H-IV, 2.2, GL H-IV, 2.4, and GL-VII, 5.4. You want to see what helps you obstruct innovation; you ignore the rest. The purpose of EPO's existence is not restriction of patents; the purpose is advancement of innovation for betterment of human condition. EPO should be regularly teaching its staff so that they don't lose sight of the purpose of their existence.

Applicant has not received a meaningful response to the complaints. Thus far EPO has only given sparse and feeble responses to serious issues. This is completely unacceptable and contrary to the interests of the public.

For example, in his letter of 09 February 2018 in response to the Formal Complaint (Attachment A) Mr. Wierzejewski simply covered up EPO improprieties and suggested that Quality Management is essentially powerless. The entire lengthy Formal Complaint with five Exhibits was dismissed in one short sentence "*We have come to the conclusion that in this case the procedure was applied in an exemplary way.*"

Further, in his letter of 22 November 2018 Mr. Wierzejewski again covered up EPO improprieties, stating that the EPC and the Guidelines for Examination were observed during the procedure. However, as noted the discussions above the EPC and the Guidelines for Examination were **not** observed during the examination of the parent and the divisional applications. Mr. Wierzejewski also stated that "allowable and patentable subject matter" has been indicated in the Divisional case at page 28 (actually page 21) of the European search opinion. However, that is not the "allowable and patentable subject matter", that is improperly restricted subject matter that will severely compromise the innovation, which has already been compromised by the EPO due the 9-yearlong prosecution of the application. For detailed rebuttals, see Applicant's response of 25 June 2019. Also as stated above in Section IV.13 and Applicant's email of 11 March 2019, patents are not charity. Applicant does not seek some "allowable subject matter," Applicant rightfully seeks protected environment for proper implementation of the extremely important innovation for public health (further elaborated below).

V. EPO's Unchecked Dominance Over European Patent System Results in Obstruction of Innovation And Fosters Stagnation

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EPO Has Monopoly Over Patent Grants In 38 EPC Countries, Giving EPO Seemingly Unchecked Dominance Over Inventors, Applicants, and Legal Representatives, Creating Perverse Incentives

A. EPO like any organization seeks to strengthen itself with more revenue at the expense of innovation and fosters stagnation

EPO is autocratic because of unchecked dominance and seeks to empower itself further with more revenue at the expense of innovation. EPO needlessly restricts patent scope and forces divisional applications because many restricted patents and more divisional applications mean more revenue for EPO. However, restricted patents and divisional applications stifle innovation for the following reasons:

i. Extra prosecution costs and delays from unnecessary restrictions which then have to be challenged under appeal, and more divisional applications are particularly burdensome for small applicant companies that form majority of EPO customers.

ii. The prosecution delays impede implementation of innovation because investors and strategic partners do not come forward until patent scope is clear. By the time the patent is granted so little patent term is left that the window to nurture the innovation in protected environment is gone (e.g., the subject case is still in prosecution 10-years after filing, during this time over $100,000 in EPO fees and legal fees have been incurred). **It should be noted that disclosure or teaching is not always enough to solve a problem. In cases such the present one, the complex innovation will not take hold in the absence of a sufficient protected term. Just like a tree sapling needs a fence around it to protect from cattle to allow growth, similarly such inventions need the twenty-year patent term for proper implementation. Therefore, the view that the patent system's objective is to induce disclosure, would be misplaced**.

iii. Many restricted patents are particularly problematic in nutrition. Thousands of patents are granted on very restricted formulations leading to advertising campaigns that cancel each other out and cause mass misinformation. This leads to total confusion and public stops believing everything.

iv. The points i-iii above lead to stagnation. Meaningful scope and timely patents are not granted; therefore, foundational problems are never solved or properly implemented. For example, in the field of lipids we have known at least since the

invention of oils 5,000 years ago[13] that lipids are important for health. In last 100 years, numerous patents have been granted either on extending shelf life (e.g. hydrogenated fats), or on structurally altering lipid molecules (e.g. hydrogenated fats), or on use of a fatty acid (e.g. omega-3) for prevention or treatment of X disease. Such solutions are often lost in the noise or cause great harm to the public (e.g. hydrogenated fats and out of context hype of omega-3). Consequently, decades later the art backtracks, for example, hydrogenated fats are now outlawed 100 years later.

Thus, by granting restricted patents and way too late, and by misplacing incentives, the EPO is making mini-solutions and creation of misinformation more financially rewarding fostering stagnation. At this rate we could stagnate for another 1000s of years without meaningful advancement in the field of nutrition.

An illustration of unnecessary restrictions in the present case is as follows: Because ED-1 improperly kept applying lack of Unity of Invention objection, on appeal to BoA the claim 1 recited above in Section II, was presented as follows in AR13.

1. A lipid-containing formulation comprising a mixture of lipids from different sources, wherein the formulation comprises a dosage of omega-6 and omega-3 fatty acids at an omega-6 to omega-3 ratio of 4:1 to 50:1, and wherein the amount of omega-3 fatty acids is between 0.1 to 30% by weight of total lipids.
2. A formulation according to claim 1, wherein the omega-6 fatty acids are 4-75% by weight of total lipids.
3. A formulation according to claim 1, wherein the dosage of omega-6 fatty acids is not more than 40 grams.
4. A formulation according to claim 1, which comprises polyunsaturated, monounsaturated, and saturated fatty acids, and the amount of omega-6 fatty acids is greater than 20% by weight of the total lipids.

However, BoA then relied upon the allegation of "added matter" to obstruct the innovation, and ED-2 copied BoA in the divisional application (discussed above).

B. Perverse Incentives Between EPO and European patent attorneys, such that rather than representing the client the attorneys represent EPO to the client

EPO holds monopoly to control patent grants in almost all European countries and with no apparent legal body above it, therefore, EPO wields unjust power and indirectly controls all European patent attorneys. The legal representatives appear more concerned about appeasing EPO officers than protecting the rights of a small company client. Moreover, both EPO and legal representatives gain in fees from prolonging the prosecution.

In the present case, Applicant's legal representatives have told the Applicant that EPO keeps track of law firms' dealings with EPO and punishes law firms unfavourable to EPO. For

[13] https://en.wikipedia.org/wiki/Vegetable_oil#History

evidence see Ms. Bhagat's testimony (Attachment A, Exhibit D paragraph [007]). Therefore, when representing a small firm (as in the subject case), legal representatives have greater incentive in going along with EPO with whom they will do business for decades representing various clients, rather than the small company that they may only represent on few cases. For evidence see incidents detailed in the Formal Compliant (pages 11-12 and 23-26) and Exhibits B and C (email exchanges with the representatives), and Exhibit D paragraphs [008], [0010]-[0015], and [0021]-[0022]. Large companies on the other hand turn tables because they can bring consistent inflow of cases to legal representatives and their own legal teams into EPO proceedings.

Therefore, for a multitude of reasons EPO has perverse incentives in alignment with legal representatives, which in particular adversely affect small companies. In such cases, client is paying the lawyer, but the lawyer is working for EPO. That is unethical and illegal.

Applicant has not experienced this degree of abuse by legal representatives in alignment/ collusion with PTO Officers in any other jurisdiction. There is something wrong about EPO practices that instill this behavior.

C. EPO Ensures That No Evidence of Its Wrongdoing is Preserved

EPO personnel take minutes of oral proceedings and rarely correct them upon requests from parties, as evidenced by Attachments B and C and evidence Exhibits C and D paragraphs [0014]-[0015] and [0020]-[0022]. Further, camera recording or sound recording are almost never allowed in the oral proceedings[14], and if allowed on rare occasions are controlled by EPO personnel.

In other words, no evidence of EPO's wrongdoing at oral proceedings can ever be preserved.

Therefore, EPO has a conflict of interest with innovation, the more it restricts patent scope, i.e. innovation, the greater its revenue; and the more it colludes with applicants' legal representatives, the more its revenue. Therefore, EPO is not only obstructing innovation, but it is fostering stagnation, counter to its charge. Again, this is contrary to the interest of the public the EPO is expected to uphold

[14] GL E-III, 8.2.1 and 10.1; and Notice of the Vice-Presidents Directorates-General 2 and 3 dated 25 February 1986, OJ EPO 1986, 63

VI. Patent-Practice-Made Humanitarian Crises

The dubious practices discussed above have created at least two kinds of humanitarian crises, first towards the public at large, and second towards independent inventors and small entities.

A. Humanitarian Rights Violations of Public at large

1. If Applicant's claims were directed to a drug candidate similarly differentiated over the prior art, the patent would have been granted many years ago (see G 2/08 holding, "patenting is also not excluded where a dosage regime is the only feature claimed which is not comprised in the state of the art"). Though EPC does not disfavour patent grant to nutrition, but EPO practice does, as evidenced above. When patents are favourably granted to drugs and devices it makes them more financially rewarding. Therefore, marketers and providers heavily tout them and make public dependent on drugs and devices. Thus, the patent practice is skewing the marketplace in favor of drugs and devices and taking public farther from prevention.

2. When nutrition patents are granted, they are severely restricted which causes confusion and makes the problem worse, as EPO is doing under the pretext of "added matter" and "unity of invention". As asserted above, piecemeal patents, particularly in the field of nutrition, do not solve problems and cannot advance nutritional arts. Rather, they create confusion by flooding the market with piecemeal product solutions that are then advertised with conflicting messages, leading to mass confusion, and canceling out of the teachings.

3. The misdirected patent policy is why public has been paying for lipid patents since 1870s (https://en.wikipedia.org/wiki/Margarine) but the problem has not gone away. The very issue is that patent protection is not provided to formulated lipid dosages for subjects, which is the necessary foundation, but patent protection is provided to different oil mixtures, or structurally altered molecules, or designing new oil varieties, which is of limited value because lipid content will still depend on where and how a species is cultivated.

4. Such missteps take us farther and farther from genuine solutions, in the meantime more harm is caused to public health. For example, it was a German patent of structurally altered fats (https://en.wikipedia.org/wiki/Wilhelm_Normann) that gave us hydrogenated fats and caused worldwide diseases for 100 years.

5. Thus, occasionally, some oils, mixtures, molecules are promoted but then they realize it does not solve the problem or causes more problems and come back to square one. The result is lipid delivery to public has not substantially advanced in 6000 years.

Because lipids are associated with health at a fundamental level, and nature is unpredictable, public suffers at a mass scale (see Section II above). It is a particular problem for impoverished populations. See Attachment A, Exhibit A.

This is a humanitarian crisis from which public has been suffering for at least 100 years, since industrialization of nutrition started to prevail. If patents were equitably granted to nutrition and drugs, then at least nutrition and prevention has a fair chance. However, in the current scenario, where EPO has compromised and sabotaged efforts such as ours with undue restrictions and 10 years of delay in patent grant, nutrition has little chance and the crisis may get more severe.

B. Humanitarian Violations of Independent inventors and Small Entities and Worldwide Effects of EPO Actions

It is extremely arduous for small entities and independent inventors to sustain such long prosecution (10 years in the present case), especially when they can get neither fair representation nor just treatment from any of the EPO's chain of command, Examining Divisions, Board of Appeal, or the Enlarged Board of Appeal, as demonstrated above.

Further, EPO's collusion with Applicant's legal representative is a *grave violation of human rights*, violating the confidence in the legal profession and justice to the very core.

Furthermore, in this case there is evidence of EPO copying USPTO's improprieties[15], and many other jurisdictions in turn have copied EPO's and USPTO's improper actions. That is *the Governments are violating independent inventors/small entities (and the public) in collusion with each other*. Because of this collusion Applicant has had to file scores of extra responses to repeated improper objections and over dozen appeals and lawsuits in various jurisdictions. Imagine the burden all these actions have placed on the small company and its proprietors, and how this has obstructed innovation and reduced the time window to implement the critical innovation.

Thankfully, some governing bodies in some other jurisdictions have demonstrated greater sense of responsibility, duty, and justice than EPO and the United States of America, thus far. For example, Intellectual Property High Court of Japan (in case of Japanese Patent application 2014-099072) and Intellectual Property Trial and Appeal Board of South Korea (in case of Korean Patent Application 10-2010-7026029) have reversed the decisions of their respective patent offices. See the respective translated decisions with the claims in Attachments K and L.

The injustice in United States has been called to the attention of the President, the Speaker, and the Congress of the United States of America. See Attachment J.

Thus, EPO practices (in collusion with other jurisdictions) have put human rights and sustainable development in jeopardy.

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[15] Alleged anticipation by individual oils was brought up for the first time by ED-1 at the Oral Proceedings held on 11 February 2015, following USPTO's allegation of anticipation by individual oils as alleged "products of nature" in the Office action of 18 August 2014 p. 14-20, in case of corresponding US patent application number 12/426,034. Additionally, BoA had raised some far-fetched objections copying the USPTO Examiner, such as referring to "different sources" as "different producer" or "different supplier." See BoA Communication of 18 April 2017; also see Attachment A, p. 17-18, 26, 31, and 32. Exhibit D paragraph [0016]-[0017]-[0022].

VII. Conclusion and Remedy Requested

Since ED-1 actions in 2015, four years have been lost in appeal and divisional application processing at the expense of innovation and public health. ED-1 and BoA successfully obstructed innovation and public well-being! They defeated the very purpose of patents, innovation for betterment of the human condition, the very reason for EPO's existence!

To what gain?

EBoA should have shown grave concern upon such violations happening at EPO that are abusive to inventors, applicants, and are sabotaging implementation of innovation for public benefit. Under the circumstances EBoA should have invalidated the oral proceedings to discourage such behaviour. Instead EBoA emboldened the actions, and ED-2 now follows in the footsteps of BoA.

This is extremely detrimental to innovation, public benefit, and EPO's charter.

How can a supra-governmental body, such as EPO, whose very reason for existence is to support innovation for betterment of the human condition obstruct such an important innovation? How can such a body be so irresponsible?

We request the Delegates in the Administrative Council take action to stop this malfeasance and request the following remedies:

1. Maintain close oversight of ED-2 actions in the divisional case along with the President for prompt grant of the case.
2. Due to EPO's malfeasance, adjust the patent term such that the 20 years patent term is counted from the date of filing of the divisional application on 21 July 2017.
3. Contemporaneous record should be taken of all oral proceedings similar to national court proceedings to avoid collusion and misconduct. At least oral proceedings at EPO should be recorded by automated video, a copy of which should be handed to the Applicant immediately at the conclusion of the oral proceedings.
4. There should be closer scrutiny of mindless added matter objections applied at EPO.
5. Reconsider revenue and reward at EPO, removing incentives for unnecessary restrictions that compromise innovation.
6. Ensure that EPO is not influencing Applicant's representatives compromising justice.
7. Extend/adjust patent terms where there are unjust delays in EPO prosecution. Such remedies exist at least at the USPTO and the Brazilian Patent Office, and quite rightly so.

Urvashi Bhagat
Chief Executive Officer