

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent of: Kirk E. Apt et al.
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Title: THRAUSTOCHYTRIDS, FATTY ACID COMPOSITIONS, AND
METHODS OF MAKING AND USES THEREOF

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**PETITION FOR *INTER PARTES* REVIEW OF UNITED STATES PATENT
NO. 10,757,959 B2 PURSUANT TO 35 U.S.C. §§ 311–319, 37 C.F.R. § 42**

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EXHIBITS

MARA-1001	U.S. Patent No. 10,757,959 B2 to Apt et al. (“the ’959 patent”)
MARA-1002	Prosecution History of the ’959 Patent (“the Prosecution History”)
MARA-1003	Declaration of Dr. Jonathan Curtis
MARA-1004	Curriculum Vitae of Dr. Jonathan Curtis
MARA-1005	RESERVED
MARA-1006	RESERVED
MARA-1007	WO 2008/129358 to Radianingtyas et al. (“Radianingtyas”)
MARA-1008	WO 97/37032 to Bijl et al. (“Bijl”)
MARA-1009	Peter D. Nichols et al., <i>New Australian Single Cell and Crop Plant Sources of Health-Enhancing Long-Chain Omega-3 Oils</i> , 13:5 Australasian Biotechnology 26 (Oct./Nov. 2003) (“Nichols-I”)
MARA-1010	Single Cell Oils: Microbial and Algal Oils (1st Ed. 2005, Cohen & Ratledge, eds.)
MARA-1011	RESERVED
MARA-1012	RESERVED
MARA-1013	RESERVED
MARA-1014	RESERVED
MARA-1015	U.S. Pat. App. Pub. No. 2004/0161831 to Komazawa et al. (“Komazawa”)
MARA-1016	RESERVED

MARA-1017	RESERVED
MARA-1018	US Pat. App. Pub. No. 2005/0273885 to Singh et al. (“Singh”)
MARA-1019	U.S. Patent No. 5,130,242 to Barclay (“Barclay”)
MARA-1020	Peter D. Nichols et al., <i>Omega-3 oils down under—An update</i> , 15:6 Inform 383 (June 2004) (“Nichols-II”)
MARA-1021	Declaration of June Munford
MARA-1022	<i>Long-Chain Omega-3 Specialty Oils</i> , H. Breivik (Ed.), The Oily Press, Bridgewater, UK (2007)
MARA-1023	<i>Fennema’s Food Chemistry</i> , S. Damodaran and K.L. Parkin (Eds.) CRC Press, Boca Raton, USA (5th ed. 2017)
MARA-1024	<i>Food Lipids</i> , C.C. Akoh and D.B. Min (Eds.), Marcel Dekker, New York, USA (2002)
MARA-1025	A.M. Burja et al., <i>Isolation and characterization of polyunsaturated fatty acid producing Thraustochytrium species: screening of strains and optimization of omega-3 production</i> , Appl. Microbiol. Biotechnol. 72: 1161-1169 (2006)
MARA-1026	RESERVED
MARA-1027	Edwin N. Frankel, <i>Lipid Oxidation</i> , The Oily Press (2005)
MARA-1028	RESERVED
MARA-1029	RESERVED
MARA-1030	WO 2009/040676 to Kralovec et al. (“Kralovec”)
MARA-1031	RESERVED
MARA-1032	Thomas Eric Lewis, <i>Characterisation and application of Australian thraustochytrids</i> , Doctoral Thesis, University of

Tasmania (June 2001)

- MARA-1033 Seshagiri Raghukumar, *Thraustochytrid Marine Protists: Production of PUFAs and Other Emerging Technologies*, Mar Biotechnol 10:631-640 (2008)
- MARA-1034 U.S. Pat. App. Pub. No. 2003/0161864 to Tanaka et al. (“Tanaka”)
- MARA-1035 W.M.N. Rainayake et al., *Preparation of Omega-3 PUFA Concentrates from Fish Oils via Urea Complexation*, 90 Jahrgang 10:381-386 (1988)
- MARA-1036 Fereidoon Shahidi and Priyatharini Ambigaipalan, *Omega-3 Polyunsaturated Fatty Acids and Their Health Benefits*, Annu. Rev. Food Sci. Technol. 9:345-81 (2018)
- MARA-1037 King-Wai Fan et al., *Lipid Characterization of Mangrove Thraustochytrid—Schizochytrium mangrovei*, J. Agric. Food Chem. 55:2906-2910 (2007)
- MARA-1038 Owen P. Ward & Ajay Singh, *Omega-3/6 Fatty Acids: Alternative Sources of Production*, Process Biochemistry 40:3627-3652 (2005)
- MARA-1039 Anthony Bimbo, *Marine Oils*, AOCS Lipid Library, <https://lipidlibrary.aocs.org/edible-oil-processing/marine-oils> (last accessed August 21, 2023).

LISTING OF CHALLENGED CLAIMS

Claim	Identifier	Claim Language
1	[1pre]	A microbial oil comprising
	[1a]	a triglyceride fraction of at least 70% by weight,
	[1b]	wherein the docosahexaenoic acid content of the triglyceride fraction is at least 45% by weight,
	[1c]	and wherein the oil comprises 1.5% by weight or less of arachidonic acid.
2	[2]	The microbial oil of claim 1, wherein said docosahexaenoic acid content of the triglyceride fraction is at least 60% by weight.
3	[3]	The microbial oil of claim 1, wherein said docosahexaenoic acid content of the triglyceride fraction is at least 80% by weight.
4	[4]	The microbial oil of claim 1, wherein said docosahexaenoic acid content of the triglyceride fraction is at least 90% by weight.
5	[5]	The microbial oil of claim 1, further comprising an arachidonic acid content of the triglyceride fraction of between 0.1% and 1.5% by weight.
6	[6]	The microbial oil of any one of claims 1 to 5, wherein said microbial oil further comprising an effective amount of at least one added antioxidant to provide oxidative stability.
7	[7]	A food product composition for animals or humans, comprising the microbial oil of any one of claims 1 to 6.
8	[8]	The food product of claim 7, wherein the food product is an infant formula.
9	[9]	The food product of claim 7, wherein the food

		product is milk, a beverage, a therapeutic drink, a nutritional drink, or a combination thereof.
10	[10]	The food product of claim 7, wherein the food product is an additive for animal or human food.
11	[11]	The food product of claim 7, wherein the food product is a nutritional supplement.
12	[12]	The food product of claim 7, wherein the food product is an animal feed
13	[13]	The animal feed of claim 12, wherein the animal feed is an aquaculture feed.
14	[14]	The animal feed of claim 12, wherein the animal feed is a domestic animal feed, a zoological animal feed, a work animal feed, a livestock feed, or a combination thereof.

Mara Renewables Corporation (“Petitioner” or “Mara”) petitions for *Inter Partes* Review (“IPR”) under 35 U.S.C. §§311–319 and 37 C.F.R. §42 of claims 1-14 (“the Challenged Claims”) of U.S. Patent No. 10,757,959 B2 (“the ’959 patent”). Compelling evidence presented in this Petition demonstrates at least a reasonable likelihood that Mara will prevail with respect to at least one Challenged Claim.

I. REQUIREMENTS FOR IPR UNDER 37 C.F.R. §42.104

A. Grounds for Standing

Mara certifies that the ’959 patent is available for IPR. Mara has not filed any civil litigation challenging the validity of the ’959 patent nor has any litigation been filed against Mara accusing it of infringing the ’959 patent. Mara is not barred or estopped from requesting this review challenging the Challenged Claims on the below-identified grounds.

B. Challenge and Relief Requested

Mara requests IPR and cancellation of the Challenged Claims on the grounds below. In support, a declaration from Dr. Jonathan Curtis (MARA-1003) is provided. MARA-1003, ¶¶1-300.

Ground	’959 Patent Claims	Basis for Rejection
Ground 1	1	Anticipated (§102) by Radianingtyas
Ground 2	1-14	Obvious (§103) over Radianingtyas and Kralovec

Ground	'959 Patent Claims	Basis for Rejection
Ground 3	1-14	Obvious (§103) over Bijl, Nichols-I and Kralovec
Ground 4	1-4, 6-14	Obvious (§103) over Bijl and Komazawa

Each applied reference pre-dates U.S. application 12/407,687, filed on March 19, 2009, the earliest filed application to which the '959 patent claims priority. Petitioner does not take a position as to whether the '959 patent is entitled to the priority date of March 19, 2009 (the "Critical Date"), but has applied references that pre-date the Critical Date and qualify as prior art, as shown below. None of the applied references were substantively opined on by the Examiner during prosecution.

Reference		Date Published	Section
Radianingtyas (MARA-1007)	WO 2008/129358	October 30, 2008	§102(a),(e)
Kralovec (MARA-1030)	WO 2009/040676	April 2, 2009	§102(e)
Bijl (MARA-1008)	WO 1997/037032	October 9, 1997	§102(b)
Nichols-I ¹ (MARA-1009)	<i>Omega-3 Oils Down Under--An Update</i> , 15 Inform 383 (June 2004)	June 2004	§102(b)
Komazawa (MARA-1015)	U.S. Pat. App. Pub. No. 2004/0161831	August 19, 2004	§102(b)

¹ Nichols-I is a printed publication that was publicly available no later than 2004.

See MARA-1021, ¶¶6-9.

C. Claim Construction

No formal claim constructions are presently necessary since “claim terms need only be construed to the extent necessary to resolve the controversy.”

Wellman, Inc. v. Eastman Chem. Co., 642 F.3d 1355, 1361 (Fed. Cir. 2011). All claim terms should be given their plain and ordinary meaning. MARA-1003, ¶¶16-17.

II. SUMMARY OF THE '959 PATENT

A. Brief Description

Generally, the '959 patent purportedly provides for specific strains of thraustochytrids (a marine microorganism) and methods and compositions for culturing, extracting, and using fatty acid oils derived from those thraustochytrids. MARA-1001 at Abstract, 3:22-24, 6:11-23. Microorganisms of the purported invention are described as containing varying fatty acids, including a triglyceride fraction of at least about 40% by weight, with varying amounts of docosapentaenoic acid n-6 (DPA n-6), eicosapentaenoic acid, heptadecanoic acid, arachidonic acid (ARA), and/or docosahexaenoic acid (DHA). MARA-1001, 3:1-10, 3:43-47, 4:1-52. Mutant/variant strains produce differing amounts of these same fatty acids. MARA-1001, 6:23-29. The '959 patent also describes methods of producing microbial oils by culturing thraustochytrids in varying conditions (such as dissolved oxygen, pH, glucose concentrations, and/or temperature) and then extracting their oils. MARA-1001, 4:41-52. Those conditions are known in

the art and encompass “conventional medium for growth of thraustochytrids.”

MARA-1001, 6:60-64; MARA-1019 (incorporated by reference).

The microbial oils of the invention extend to “any oil derived from a microorganism,” which includes “a crude oil,” a “refined oil that is obtained by treating a crude microbial oil,” a “diluted microbial oil obtained by diluting a crude or refined microbial oil,” and “an enriched oil” obtained “by treating a crude or refined microbial oil with further methods of purification to increase the concentration of a fatty acid (such as DHA) in the oil.” MARA-1001, 10:31-42. These oils may then be applied in compositions, such as in “food products, pharmaceutical compositions, cosmetics, and industrial compositions.” MARA-1001, 15:19-21; MARA-1003, ¶¶49-53.

The ’959 patent includes 14 claims, of which claim 1 is independent. MARA-1003, ¶54.

B. Summary of the Prosecution History of the ’959 Patent

U.S. 10,757,959 issued on September 1, 2020 from U.S. Patent Application No. 16/132,992 (“the ’992 application”), filed on September 17, 2018 as a divisional application. *See* MARA-1002; MARA-1003, ¶55.

During prosecution, the Examiner issued a single substantive rejection, rejecting all but claim 55 over Fichtali et al., U.S. Pat. Pub. No. 2007/0003686. The Examiner noted that Fichtali “does not mention heptadecanoic acid,” and

suggested that “the claims may be amended around the cited reference by adding to claim 51 the limitation that the amount of heptadecanoic acid is between 0.1% and 5% by weight (i.e., not zero).” MARA-1002, 158-159. Further, the Examiner noted that claim 55 was allegedly “free of the prior art” because the prior art disclosed that “the amount of ARA is not 1.5% or less by weight.” *Id.*, 158. In response, Patentee amended claim 51 (issued claim 1) to recite less than 1.5% of ARA. *Id.*, 194.

Patentee also argued that Fichtali did not disclose fatty acids in the triglyceride form or in an amount claimed by the patent. *Id.*, 192. With that amendment, the Examiner allowed the claims. *Id.*, 198-204; MARA-1003, ¶¶57-60.

C. The Effective Priority Date of the Claims of the '959 Patent

The '959 patent issued from U.S. Application No. 16/132,992, filed on September 17, 2018. The '959 patent is a divisional patent; it traces its history back to U.S. Patent Application No. 12/407,687, filed on March 19, 2009, which is now U.S. Patent No. 8,207,363.

Claim 1 of the '959 patent is an independent claim. Claims 2-14 depend directly or indirectly from claim 1. Accordingly, claims 2-14 cannot enjoy an effective filing date earlier than that of claim 1 from which they depend (*i.e.*, no earlier than March 19, 2009). *See* MARA-1003, ¶¶61-62.

D. Level of Ordinary Skill in the Art

A person having ordinary skill in the art relating to the subject matter of the '959 patent as of March 19, 2009 (a "PHOSITA") would have had a Master of Science degree in an academic discipline emphasizing chemistry, chemical engineering, or biochemistry, in combination with training or at least two to three years of related work experience with lipid chemistry technologies, including but not limited to lipid extraction technologies. MARA-1003, ¶¶63-64. Alternatively, the person could have also had a Doctorate degree in a relevant academic discipline with one to two years of related work experience in the same discipline. *Id.*

A PHOSITA would have been familiar with microbial oils, a summary of which Dr. Curtis provides in his declaration. *See* MARA-1003, ¶¶36-48, 64. In particular, a PHOSITA would have understood the benefits of polyunsaturated fats (PUFAs), microbial sources for obtaining them, and methods for culturing and extracting oils from those microbial sources. *Id.*, ¶64.

III. THE CHALLENGED CLAIMS ARE UNPATENTABLE

This request shows how the prior art discloses each of the elements of the Challenged Claims, thereby rendering claims 1-14 of the '959 patent unpatentable. *See also* MARA-1003, ¶¶15, 65. As detailed below, this request shows a reasonable likelihood that Mara will prevail with respect to claims 1-14 of the '959

patent.

A. GROUND 1: Claim 1 is anticipated by Radianingtyas

1. Overview of Radianingtyas

Radianingtyas, like the '959 patent, is directed to methods of culturing oil-producing microbes and extracting microbial oils rich in omega-3 and omega-6 fatty acids. MARA-1007, 1:27-2:2; MARA-1001, 1:27-32, 1:63-2:18, 2:33-52, 10:16-14:24. The method of Radianingtyas includes collecting cell biomass, breaking or disrupting that biomass, and then extracting the biomass with solvents such as “chloroform, hexane, methanol, ethanol or via supercritical fluid extraction means.” MARA-1007, 32:10-14; MARA-1003, ¶¶66.

Radianingtyas's resultant oils comprise unsaturated fatty acids with approximately 96-100 wt.% triglycerides in the neutral lipid fraction, where the percentage of neutral lipids “can be at least 95% by weight of total lipids.” MARA-1007, 32:20-21, 33:1-2. Constituent acids include DHA as well as low levels of ARA. *Id.*, 11:4-9, 99:22-24, 99:29-32. As Radianingtyas discloses, naturally-occurring microorganisms produce microbial oils with “high concentrations of omega-3 fatty acids...and low concentrations of omega-6 fatty acids.” *Id.*, 12:22-25; *see also id.*, 13:7-10, 17:19-20, 40:2-4; MARA-1003, ¶¶67-68. Additionally, the microbial oils produced by Radianingtyas's microorganisms “can also produce antioxidants,” and the oils and antioxidants can be produced

“both individually and cumulatively.” MARA-1007, 11:10-21; *see also id.*, 18:4-20:4, 37:24-39:24, 89:32-90:25.

Depending on one’s goals, the method parameters of Radianingtyas can be modified to obtain different yields of DHA. MARA-1007, 27:4-8. Radianingtyas explains that modifying the “medium of an oil producing microbe with a fatty acid production antagonist” will increase the “ratio of omega n-3 and/or n-6 oils to omega n-9 oils,” as will manipulation of carbon-to-nitrogen sources and “by the addition of certain chemical compounds which impact upon fatty acid production.” *Id.*, 27:15-28. More specifically, Radianingtyas teaches that increases in agitation, temperature, or dissolved oxygen during culturing decrease DHA content, while additions of acetate, trace elements, metal, and vitamins to the production medium increase DHA content. *Id.*, 28:14-20, 30:15-17; MARA-1003, ¶¶69-70.

As one example, Radianingtyas discloses a specific strain of Thraustochytrids (i.e. a marine microorganism) labeled ONC-T18. *See* MARA-1007, 16:1-20:23, 26:29-27:3, 81:5-92:2; MARA-1003, ¶71. Radianingtyas discloses that “the fatty acid component which ONC-T18 produces under heterotrophic fermentation is almost entirely triglyceride (*at least 95%*) in nature.”² MARA-1007, 89:24-26. Further, Radianingtyas discloses that microorganisms such as ONC-T18 can produce “a lipid composition comprising from about 25% to

² All emphasis added herein unless otherwise noted.

about 40% of an omega-3 fatty acid, such as n-3 DHA, (for example, at least 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55% or 60% by weight).” MARA-1007, 26:29-34. ONC-T18 can also produce antioxidants. *See* MARA-1007, 89:32-90:25 (section titled “Example 7: Production of antioxidants using the strain, ONC-T18”).

2. Analysis

Claim 1

[1pre] A microbial oil comprising

Radianingtyas discloses [1pre]. MARA-1003, ¶¶72-76. Radianingtyas describes “compositions and methods related to oil producing microbes that can produce unsaturated fatty acids which can be purified and used.” MARA-1007, Abstract; *id.*, 12:1-2 (“Also disclosed are processes for the production of microbial derived (or single celled) oils.”), 1:27-31 (“Disclosed are compositions and methods related oil producing microbes, which when cultured produce... omega 3 (n-3) and/or omega 6 (n-6) oils, such as DHA, EPA and DPA”), 1:22-26, 40:29-31.

Radianingtyas discloses that “[c]ellular lipids containing the (n-3) DHA, EPA and (n-6) DPA PUFAs can...be extracted from the cellular biomass...to produce a sample of concentrated lipid material.” *Id.*, 42:10-14; *see also id.*, 32:10-14, 42:10-43:10; MARA-1003, ¶¶74-75.

[1a] a triglyceride fraction of at least 70% by weight,

Radianingtyas discloses [1a]. MARA-1003, ¶¶77-80.

For example, Radianingtyas generally discloses “oil producing microbes of the order Thraustochytriales...having the ability to produce lipids” containing “omega-3 fatty acids” and “omega-6 fatty acids.” MARA-1007, 11:4-9.

Radianingtyas’s compositions include triglycerides from “96 to about 100%” of the neutral lipids, which “can be at least 95% by weight of total lipids.” MARA-1007, 32:17-33:5; *see also id.*, 89:24-26; MARA-1003, ¶78.

More specifically, Radianingtyas discloses the strain ONC-T18, of which “[a]nalysis of results shows that the fatty acid component which ONC-T18 produces under heterotrophic fermentation *is almost entirely triglyceride (at least 95%)* in nature.” MARA-1007, 89:24-26; MARA-1003 ¶79.

[1b] wherein the docosahexaenoic acid content of the triglyceride fraction is at least 45% by weight,

Radianingtyas discloses [1b]. MARA-1003, ¶¶81-86.

Radianingtyas discloses examples that result in the “[o]ptimized production of [DHA] by strain ONC-T18” and show the “[o]ptimal time for harvesting of ONC-T18 for maximal DHA production.” MARA-1007, 87:6-89:10. Further, Radianingtyas discloses that microorganisms “such as ONC-T18...can produce a lipid composition comprising from about 25% to about 40% of an omega-3 fatty acid, such as n-3 DHA, (for example, at least...40%, 45%, 50%, 55% or 60% by weight).” MARA-1007, 26:29-34. The fatty acid component that ONC-T18 produces is “at least 95%” triglyceride, so in an oil containing 60% DHA (as

contemplated by Radianingtyas), even if the remaining 5% fatty acid component that was not in triglyceride form was entirely DHA, the oil would still contain 55% DHA in triglyceride form and would still meet [1b]. MARA-1003, ¶¶81-84. Moreover, a PHOSITA would also have understood that because the majority of Radianingtyas's microbial oils are made up of triglycerides (e.g., up to 100%), the majority of the PUFAs in Radianingtyas would be present in the triglyceride form. MARA-1003, ¶83.

Finally, Radianingtyas also teaches that extracted oils can be further purified to increase DHA content. *See* MARA-1007, 8:2-4 (“For example, if a disclosed eukaryotic microorganism, for example, produces 35% DHA, this could be further ‘purified’ such that the final lipid composition was greater than 90% DHA.”); MARA-1003, ¶85.

[1c] and wherein the oil comprises 1.5% by weight or less of arachidonic acid.

Radianingtyas discloses [1c]. MARA-1003, ¶¶87-91.

Radianingtyas discloses exemplary oils that contain 1.5% by weight or less ARA. For instance, in Example 13, titled “Isolation and characterization of [PUFA] producting[sic] *Thraustochytrium* sp. ONC-T18,” Radianingtyas discloses that “[i]n addition to the omega-3 oils produced, approximately 80% of all isolates synthesized the omega-6 PUFAs, arachidonic acid (AA)...at concentrations varying between 1 and 18%.” MARA-1007, 96:1-3, 99:29-32, Fig. 11. “A prior

art reference that discloses an overlapping but different range than the claimed range can be anticipatory, even where the prior art range only partially or slightly overlaps with the claimed range.” *Genentech, Inc. v. Hospira, Inc.*, 946 F.3d 1333, 1338 (Fed. Cir. 2020); *see also Ineos USA LLC v. Berry Plastics Corp.*, 783 F.3d 865, 870–71 (Fed. Cir. 2015) (affirming summary judgment of anticipation of patent claims for composition with “0.05 to 0.5% by weight of at least one saturated fatty acid amide” lubricant in view of a prior art reference disclosing the same class of lubricant in an overlapping range of “0.1 to 5 parts by weight,” and the parties agreed that a measurement in “% by weight” was equivalent to one in “parts by weight”).

Additionally, Radianingtyas also discloses that its oil producing microbes can produce a wide range of oils that all consistently contain low amounts of ARA. *See* MARA-1007, 34:4-37:14 (showing ARA ranging from 0.13% to 0.90% as percentage of total fatty acid). In some embodiments, ARA is not disclosed at all, and is either absent or below the limit of detection. *See, e.g.*, MARA-1007, 32:20-25 (“typical composition of fatty acids for ONC-T18, in the neutral lipids” summing to 100% without disclosing ARA). As described in more detail in Section III.C.3 below, “1.5% by weight or less” includes compositions with 0% ARA.

Therefore, Radianingtyas anticipates claim 1.

B. GROUND 2: Claims 1-14 are obvious over Radianingtyas in view of Kralovec

1. Overview of Radianingtyas

See Section III.A.1, *supra*.

2. Overview of Kralovec

Kralovec relates to methods for modifying oil compositions in microbial oils by concentrating polyunsaturated fatty acids. MARA-1030, 1:9-11. Kralovec recognizes that omega-3 fatty acids like DHA have “well established” beneficial effects, such as reduction of “cardiovascular and heart disease risk” and “prevention and/or treatment of inflammation, neurogenerative diseases, and cognitive development.” MARA-1030, 1:16-2:3. Kralovec also acknowledges that omega-3 fatty acids can be found in microbial and algal oils, which “typically provide the PUFA in a triglyceride form where other undesired, fatty acids...are present along side a desired PUFA in the triglyceride molecule.” *Id.*, 2:4-8. Kralovec is thus directed to a modification method to produce “an oil having higher levels of a PUFA...than the starting oil composition.” *Id.*, 5:24-28; MARA-1003, ¶93.

The Kralovec method can be broadly used with “any suitable oil composition that comprises a glyceride,” including microbial and algal oils. *Id.*, 6:28-7:2. Kralovec’s methods allow the “specific composition of a treated oil” to be “adjusted and/or tailored to have a target ratio of various polyunsaturated fatty

acids,” which can allow for “high concentrations of DHA.” *Id.*, 6:9-13; MARA-1003, ¶94.

Kralovec’s method employs three steps: hydrolysis, separation, and esterification. MARA-1003, ¶95. Hydrolysis utilizes enzymatic lipase to contact a starting oil, which induces hydrolysis of the oil. *Id.*, 9:8-10. This process creates hydrolyzed glycerides and free saturated fatty acids. *Id.* Using modifications such as atmospheric conditions, mixing/agitation, or elevated temperature, a user induces a “desired amount of hydrolysis.” *Id.*, 11:15-28. Then, the “hydrolyzed glyceride composition...can then be separated...to separate at least a portion of the free saturated fatty acid from the glyceride.” *Id.*, 12:13-16. After, lipase is utilized to attach “desirable polyunsaturated fatty acid components, for example, EPA and/or DHA” to the hydrolyzed glyceride compositions. *Id.*, 13:27-30. This method provides compositions containing “triglycerides with higher DHA...contents than the starting triglycerides.” *Id.*, 35:20-32; MARA-1003, ¶¶95-97.

3. Combination of Radianingtyas and Kralovec

a) DHA as the preferred PUFA

As discussed above (§III.A.1, *supra*), Radianingtyas teaches methods of culturing oil-producing microbes and extracting microbial oils rich in omega-3 and omega-6 fatty acids. MARA-1007, 1:27-2:2; MARA-1001, 1:27-32, 1:63-2:18,

2:33-52, 10:16-14:24. More specifically, Radianingtyas discloses examples directed to “[o]ptimized production of [DHA] by strain ONC-T18” and “[o]ptimal time for harvesting of ONC-T18 for maximal DHA production.” MARA-1007, 87:6-89:10. In light of Radianingtyas’s disclosures, it would have been obvious for a PHOSITA to have sought microbial oils having high levels of DHA as the preferred PUFA based on its teachings as well as those of other references available before the Critical Date. MARA-1030, 1:9-11; MARA-1003, ¶¶98-104. A PHOSITA would have been motivated to obtain increased DHA in Radianingtyas’s extracted microbial oil for at least the following reasons.

First, a PHOSITA would have been motivated to increase DHA in Radianingtyas’s extracted microbial oil because there were many recognized health benefits associated with DHA. MARA-1003, ¶¶100-101. For example, Radianingtyas teaches that “[t]here is overwhelming scientific evidence that (n-3) highly unsaturated fatty acids such as docosahexaenoic acid (DHA) have a positive effect on cardio-circulatory diseases, chronic inflammations and brain disorders[.]” MARA-1007, 1:6-8. Similarly, Kralovec teaches that DHA was known to reduce “cardiovascular and heart disease risk” and was crucial to the “prevention and/or treatment of inflammation, neurogenerative diseases, and cognitive development.” MARA-1030, 1:16-2:3. Kralovec also teaches that DHA was associated with “a strong insulin permeability enhancement effect” and was “viewed as a potential

absorption enhancer for intestinal delivery of insulin.” MARA-1030, 18:10-19:2.

For example, DHA was understood to “prevent[] certain biochemical processes that originate from insulin deficiency” and “significantly increase fasting insulin levels.” MARA-1030, 19:2-6.

Second, a PHOSITA would have been motivated to increase DHA content in Radianingtyas’s microbial oil because Kralovec teaches that DHA is an omega-3 fatty acid, known to be “vital to everyday life and function.” MARA-1030, 1:13-14; MARA-1003, ¶102. For example, “[o]mega-3 fatty acids not only exhibit proven effects on lowering serum triglyceride levels, but they have strong connection to diabetes.” MARA-1030, 18:8-12. Omega-3 fatty acids were also “known for other cardioprotective benefits,” such as “reduc[ing] cardiovascular and heart disease risk.” MARA-1030, 1:13-2:3.

Third, a PHOSITA would have been motivated to focus on increasing DHA in Radianingtyas’s oil because DHA would have been an obvious choice selected from a small and finite number of preferred omega-3 fatty acids. *In re Kuhle*, 526 F.2d 553, 555 (C.C.P.A. 1975); MARA-1003, ¶103. For example, Radianingtyas discloses DHA as one of the two desirable n-3 PUFAs: docosahexaenoic acid (DHA, 22:6 n-3) and eicosapentaenoic acid (EPA, 20:5 n-3). MARA-1007, 1:6-20; MARA-1003, ¶103.

A PHOSITA would have expected to be successful in pursuing increased DHA in an extracted oil because Radianingtyas identifies DHA as one of two desirable PUFAs. MARA-1007, 1:6-20; MARA-1003, ¶¶103-104. Moreover, a PHOSITA would have expected success in pursuing extracted oils with high levels of DHA given that it was already known that certain strains of microbes contained “very high levels of DHA (61%).” MARA-1009, 27; MARA-1003, ¶104.

b) Increased Omega-3 Fatty Acid (DHA) Concentration in Microbial Oils

Radianingtyas teaches suitable starting oils that have not been treated, such as microbial oils from organisms that “can be used in a process for preparing a lipid or fat containing DHA, EPA and DPA.” MARA-1007, 16:31-17:3. As discussed above (§III.B.2, *supra*), Kralovec provides methods for obtaining compositions containing “triglycerides with higher DHA...contents than the starting triglycerides.” MARA-1030, 35:20-32. It would have been obvious for a PHOSITA to combine the teachings of Radianingtyas, directed to microbial oils having high levels of triglycerides (e.g., approximately 96-100%) and DHA (at least 60% by weight), with Kralovec, directed to methods for modifying an oil composition, to increase the concentration of DHA in the microbial oil. MARA-1007, 26:31-34, 33:1-2; MARA-1030, 1:9-11; MARA-1003, ¶¶105-106. Specifically, a PHOSITA would have found it obvious to implement Kralovec’s oil modification techniques (or similar) to Radianingtyas’s extracted microbial oil to

increase the amount of DHA for at least the following reasons.

First, a PHOSITA would have been motivated to apply Kralovec's oil modification techniques to Radianingtyas's extracted microbial oil to increase its DHA content because "purifying and concentrating PUFA's [sic] in a triglyceride form is generally desired." MARA-1030, 2:7-8; MARA-1003, ¶107. It would have been well-known that decreasing the amount of unwanted components in a microbial oil would be desirable because "[p]olyunsaturated fatty acids, such as, for example omega-3 fatty acids, are often derived from marine oils, microbial, and/or algal oils," which "typically provide the PUFA in a triglyceride form where other undesired, fatty acids...are present along side a desired PUFA in the triglyceride molecule." MARA-1030, 2:4-8; MARA-1003, ¶107.

Second, a PHOSITA would have been motivated to apply Kralovec's oil modification techniques to Radianingtyas's extracted microbial oil to increase its DHA content because the produced oils include "'designer' glycerides" and "often non-naturally occurring, ratios of polyunsaturated fatty acid ester" that provide "triglycerides that have better color and lower levels of trans-isomers" as well as "better sensory properties." MARA-1030, 35:21-36:2; MARA-1003, ¶108. "Such oils can be incorporated into food products, nutraceuticals, pharmaceutical formulations, and microcapsules." MARA-1030, 35:21-36:2.

Third, a PHOSITA would have been motivated to apply Kralovec's oil

modification techniques to Radianingtyas's extracted microbial oil because such combinations reflect nothing more than the use of a known technology (e.g., enzymatic modification) to improve similar oils (e.g., extracted microbial oils) according to known methods (e.g. oil refinement methods) to yield predictable results (e.g., obtain oil with an increased concentration of a desired PUFA, e.g., DHA). *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007); MARA-1003, ¶109.

A PHOSITA would have expected to be successful in applying Kralovec's techniques to increase the concentration of DHA in the microbial oil because Radianingtyas teaches that "[t]he omega-3 and omega-6 PUFAs may be further concentrated by hydrolyzing the lipids and concentrating the highly unsaturated fraction by employing traditional methods." MARA-1007, 42:14-16; *see also id.*, 42:19-20 ("The extracted oils can be refined by well-known processes"); MARA-1003, ¶110. A PHOSITA would have naturally considered "traditional" or "well-known" methods for modifying an oil such as Radianingtyas's oil, including Kralovec's methods or similar. MARA-1003, ¶¶110-111. Thus, a PHOSITA would have looked to refine Radianingtyas's oils in accordance with Radianingtyas's teachings by looking to Kralovec. MARA-1003, ¶111.

Moreover, a PHOSITA would have expected success in using Kralovec's method techniques for increasing the concentration of the preferred PUFA (i.e.,

DHA) particularly in the context of an extracted microbial oil given that Radianingtyas and Kralovec teach that their oils are microbial/algal in origin and so have similar characteristics. MARA-1007, 1:22-31; MARA-1030, 2:28-29; MARA-1003, ¶112. Both acknowledge their oils are specific to containing omega-3 PUFAs, and even more specifically DHA. MARA-1007, 1:22-31; MARA-1030, 19:7-12. Furthermore, both Radianingtyas and Kralovec acknowledge similar uses for their oils, such as human nutritional uses. Radianingtyas, for example, teaches that its resultant oil is “used as a nutritional supplements[sic] for humans, as a food additive, or as pharmaceutical applications.” MARA-1007, 43:6-8. Kralovec too discloses that its oils “can be incorporated into food products, nutraceuticals, pharmaceutical formulations, and microcapsules.” MARA-1030, 35:31-36:2; MARA-1003, ¶¶113-114.

4. Analysis

Claim 1

[1pre] A microbial oil comprising

Radianingtyas-Kralovec discloses and/or renders obvious [1pre]. MARA-1003, ¶¶115-117.

Radianingtyas discloses [1pre]. *See* Section III.A.2[1pre], *supra*. Kralovec also discloses that its methods can be used with microbial oils. *See, e.g.*, MARA-1030, 6:28-7:2; MARA-1003, ¶116. Additionally, extracted microbial oils were well known to a PHOSITA prior to the Critical Date. For example, other prior art

references, such as Barclay, describe an extracted microbial oil. *See* MARA-1019, 1:23-28. It describes an “oil consisting of a simple fatty acid profile such as that produced by Thraustochytrids,” as well as oils produced from *Schizochytrium*, also a microbe. *Id.*, 14:23-47. Contemporaneous literature describes that Barclay’s work employed “technology for DHA production from thraustochytrids,” which included “microbial production of single cell oil.” MARA-1033, 632. And at the same time, thraustochytrids were known as a source of “oils with a suite of PUFA profiles that can have specific uses,” including “*Schizochytrium* oil, known as DHA Gold, [which was] marketed by Omega Tech Inc to supplement animal feeds.” *Id.*, 631, 635; MARA-1003, ¶¶117.

[1a] a triglyceride fraction of at least 70% by weight,

Radianingtyas-Kralovec discloses and/or renders obvious [1a]. MARA-1003, ¶¶118-121.

Radianingtyas discloses [1a]. *See* Section III.A.2[1a], *supra*. Similarly, Kralovec discloses oils that “have a high TG (triglyceride) content,” for example, “the oil can comprise greater than or equal to about 60%, 65%, 70%, 75%, or 80% TG by weight of the total composition.” MARA-1030, 37:22-24; *see also id.*, 36, tbl.5 (disclosing “TG content” of “60-80%” “after the disclosed hydrolysis and esterification”); MARA-1003, ¶119.

Indeed, triglyceride-rich oils were well known to a PHOSITA prior to the

Critical Date. Consistent with the teachings in Radianingtyas and Kralovec, other references (e.g., Singh) also disclosed triglyceride-rich oils. MARA-1018, [0294] (“oil comprising at least 75% or 85% triacylglycerols...said triacylglycerols comprising the LC-PUFA”); MARA-1003, ¶¶120-121.

[1b] wherein the docosaehaenoic acid content of the triglyceride fraction is at least 45% by weight,

Radianingtyas-Kralovec discloses and/or renders obvious [1b]. MARA-1003, ¶¶122-123.

Radianingtyas discloses [1b]. *See* Section III.A.2[1b], *supra*. Radianingtyas discloses that microorganism ONC-T18 can produce a lipid composition comprising an omega-3 fatty acid, such as n-3 DHA in an amount of “at least . . . 40%, 45%, 50%, 55% or 60% by weight.” MARA-1007, 26:29-34. Additionally, a PHOSITA would have understood and/or found obvious to apply Kralovec’s (or similar) methods to the Radianingtyas microbial oil to produce a DHA-enriched microbial oil containing at least 45 wt.% DHA, or higher, such as at least 60 wt.% DHA or at least 80 wt.% DHA in triglyceride form. MARA-1003, ¶123. That in turn discloses or renders obvious [1b]. *Id.*

[1c] and wherein the oil comprises 1.5% by weight or less of arachidonic acid.

Radianingtyas-Kralovec discloses and/or renders obvious [1c]. MARA-1003, ¶¶124-127.

Radianingtyas discloses [1c]. *See* Section III.A.2[1c], *supra*. It would have been obvious to a PHOSITA that Radianingtyas's oil has 1.5% by weight or less ARA because in Example 13, regarding the isolation of strain ONC-T18, Radianingtyas discloses that "approximately 80% of all isolates synthesized the omega-6 PUFAs, arachidonic acid (AA)...at concentrations varying between 1 and 18%." MARA-1007, 96:1-3, 99:29-32; *see also id.*, Fig. 11. Additionally, Radianingtyas discloses production of a wide range of oils with consistently low amounts of ARA. *See* MARA-1007, 34:4-37:14. In some embodiments, ARA is not detectable at all. *See, e.g., id.*, 32:20-25. As described in more detail in Section III.C.3 below, "1.5% by weight or less" includes compositions with 0% ARA.

Additionally, Kralovec teaches that in an embodiment using Kralovec's method for increasing DHA, ARA is present at no more than 1.4% of the glyceride fraction. MARA-1030, 43-44 & tbl.9.1; *see also* MARA-1019, tbl.3 (indicating 72.7% DHA and 0% ARA); MARA-1003, ¶125.

Moreover, a PHOSITA would have understood that it was desirable to have low levels of ARA in a primarily DHA-containing oil. As motivation, a PHOSITA would recognize that high-DHA, low-ARA concentrations would be preferable to DHA from fish oil because of "the low content of the desired fatty acids" in fish oils. MARA-1034, [0005]; MARA-1003, ¶¶125-126. A PHOSITA would have

therefore wanted to achieve a high-purity, DHA-containing oil free of contaminants or other PUFAs for more efficient supplementation of human and animal food products. Indeed, a higher-purity, DHA-containing oil would be preferable because it results in a consumer needing to take fewer supplements (i.e. capsules) and reduces the “calories ingested from unwanted fatty acids.” MARA-1022, 113; MARA-1035, 381 (“Concentrates keep the intake of calories and other possibly physiologically active fatty acids as low as possible.”). Thus, a PHOSITA would have sought out microbial oils containing low amounts of ARA. MARA-1003, ¶¶126-127.

Therefore, Radianingtyas-Kralovec renders obvious claim 1.

Claim 2

[2] The microbial oil of claim 1, wherein said docosahexaenoic acid content of the triglyceride fraction is at least 60% by weight.

Radianingtyas-Kralovec discloses and/or renders obvious [2]. MARA-1003, ¶¶128-136.

Radianingtyas discloses examples that result in the “[o]ptimized production of [DHA] by strain ONC-T18” and show the “[o]ptimal time for harvesting of ONC-T18 for maximal DHA production.” MARA-1007, 87:6-89:10. Further, Radianingtyas discloses that microorganisms “such as ONC-T18...can produce a lipid composition comprising from about 25% to about 40% of an omega-3 fatty acid, such as n-3 DHA, (for example, at least . . . 40%, 45%, 50%, 55% or 60% by

weight).” MARA-1007, 26:29-34. Because the fatty acid component that ONC-T18 produces is “at least 95%” triglyceride, in the unlikely circumstance that the remaining 5% fatty acid component that was not in triglyceride form was entirely DHA, the oil would still contain 55% DHA (i.e. nearly 60% DHA) in triglyceride form. But a PHOSITA would also have understood that because the majority of Radianingtyas’s microbial oils are made up of triglycerides (e.g., up to 100%), the majority of the PUFAs in Radianingtyas would be present in triglyceride form, including the DHA. MARA-1003, ¶¶128-130.

Additionally, compositions having a DHA content of the triglyceride fraction that is at least 60% by weight were also well known to a PHOSITA based on the prior art that was available before the Critical Date. MARA-1003, ¶131. Radianingtyas generally discloses “oil producing microbes...preferably *Thraustochytrium*... having the ability to produce lipids...unsaturated fatty acids...such as...DHA.” MARA-1007, 11:4-9. It was known prior to the Critical Date that there were microorganisms of a *Thraustochytrium* strain that had “a high ability of producing docosahexaenoic acid” and were producing oil with at least 60% by weight DHA. MARA-1015, Abstract; *see also id.*, [0016], [0051], [0116], Fig. 3; MARA-1009, 27; MARA-1032, 27-31. It was also known how to increase the yield of desired fatty acids, including DHA. For example, it was known that

decreasing agitation or dissolved oxygen during culturing would result in increases of DHA. MARA-1007, 28:15-17, 27:13-21; MARA-1003, ¶131.

To the extent the DHA content in the triglyceride fraction in Radianingtyas's microbial oil is determined to be less than 60%, Radianingtyas teaches that "if a disclosed eukaryotic microorganism, for example, produces 35% DHA, this could be further 'purified' such that the final lipid composition was greater than 90% DHA." MARA-1007, 8:2-4; MARA-1003, ¶¶131-132.

Additionally, a PHOSITA would also readily know how to increase the DHA content in triglyceride form using methods disclosed in references like Kralovec. As discussed above (§III.B.3, *supra*), in the combination, a PHOSITA would have been motivated to apply Kralovec's oil modification techniques (or similar) to Radianingtyas's extracted microbial oil to increase its DHA content. MARA-1003, ¶133. In doing so, Kralovec discloses its methods can be used to produce "concentrated oils with triglycerides containing higher proportions of polyunsaturated fatty acid esters than the starting glycerides," such as "oils that comprise greater than or equal to about...80% DHA by weight of the total composition." MARA-1030, 35:20-27, 36:12-15. Such oils would "also have a high TG (triglyceride) content" and the method would "produce triglycerides of fatty acids." MARA-1030, 35:27-30, 37:22. The end result would be "an oil

having higher levels of a PUFA...than the starting oil composition.” MARA-1030, 5:24-32.

A PHOSITA would have therefore understood and/or found obvious to apply Kralovec’s (or similar) methods to Radianingtyas’s microbial oil to produce a DHA-enriched microbial oil containing at least 60 wt.% DHA in triglyceride form. MARA-1003, ¶¶134-135. As Dr. Curtis explains, a PHOSITA would understand that having higher levels of DHA in triglyceride form was desirable because it would mean a more homogeneous oil, desirable for use in pharmaceutical preparations. MARA-1003, ¶136. Additionally, the presence of phospholipids, as opposed to triglycerides, was known to make oils less stable, more cloudy, and more difficult to process efficiently. *Id.* Moreover, when enrichment of DHA is performed via conversion to the ethyl ester form followed by distillation (a commercially important process), the resulting ethyl ester-form DHA concentrates can be considered as an “unnatural form.” *Id.* In contrast, providing high levels of DHA in the triglyceride form more closely resembles the “natural” form in which lipids are predominantly ingested. *Id.* Hence, the triglyceride form of DHA would be expected to have greater consumer acceptability, along with the possibility of greater bioavailability according to some literature. *See* MARA-1036, 352-354, tbl.2; MARA-1003 ¶136.

Claim 3

[3] The microbial oil of claim 1, wherein said docosahexaenoic acid content of the triglyceride fraction is at least 80% by weight.

Radianingtyas-Kralovec discloses and/or renders obvious [3]. MARA-1003, ¶¶137-147.

Compositions having a DHA content of the triglyceride fraction that is at least 80% by weight were known to a PHOSITA based on the prior art that was available before the Critical Date. MARA-1003, ¶¶138-142. Radianingtyas generally discloses “oil producing microbes...preferably *Thraustochytrium*... having the ability to produce lipids...unsaturated fatty acids...such as...DHA.” MARA-1007, 11:4-9. It was known prior to the Critical Date that there were microorganisms of a *Thraustochytrium* strain that had “a high ability of producing docosahexaenoic acid” and were producing oil with at least 60% by weight DHA. MARA-1015, Abstract; *see also id.*, [0016], [0051], [0116], Fig. 3; MARA-1009, 27; MARA-1032, 27-31; MARA-1003, ¶¶141-142.

As described in Sections III.B.3 and III.B.4[2], *supra*, it was also known how to increase the yield of desired fatty acids such as DHA using methods like those disclosed in Kralovec, and it was further known that doing so would produce a desirable oil. MARA-1003, ¶¶143-146. For example, it was known that decreasing agitation or dissolved oxygen during culturing would result in increases of DHA. MARA-1007, 28:15-17, 27:13-21. Additionally, Radianingtyas itself discloses that “if a disclosed eukaryotic microorganism, for example, produces

35% DHA, this could be further ‘purified’ such that the final lipid composition was greater than 90% DHA.” *Id.*, 8:2-4; MARA-1003, ¶¶143.

Further, as previously described, a PHOSITA would also readily know how to increase the DHA content in triglyceride form using methods disclosed in references like Kralovec. MARA-1003, ¶¶144-145; MARA-1030, 5:24-32, 35:20-30, 36:12-15, 37:22.

A PHOSITA would have therefore understood and/or found obvious to apply Kralovec’s (or similar) methods to Radianingtyas’s microbial oil to produce a DHA-enriched microbial oil containing at least 80 wt.% DHA in triglyceride form. MARA-1003, ¶146. A PHOSITA would understand that having higher levels of DHA in triglyceride form was desirable for the stability and consumer acceptability reasons discussed above in Sections III.B.3 and III.B.4[2]. MARA-1003, ¶147.

Claim 4

[4] The microbial oil of claim 1, wherein said docosahexaenoic acid content of the triglyceride fraction is at least 90% by weight.

Radianingtyas-Kralovec discloses and/or renders obvious [4]. MARA-1003, ¶¶148-155.

Compositions having a DHA content of the triglyceride fraction that is at least 90% by weight were known to a PHOSITA based on the prior art that was available before the Critical Date. MARA-1003, ¶¶148-149; *see also* Section

III.B.4[3], *supra*. Radianingtyas teaches that “if a disclosed eukaryotic microorganism, for example, produces 35% DHA, this could be further ‘purified’ such that the final lipid composition was greater than 90% DHA.” MARA-1007, 8:2-4; MARA-1003, ¶¶149.

As described in Sections III.B.3 and III.B.4[2], *supra*, it was also known how to increase the yield of desired fatty acids such as DHA using methods like those disclosed in Kralovec, and it was further known that doing so would produce a desirable oil. MARA-1003, ¶¶152-154; MARA-1030, 5:24-32, 35:20-30, 36:12-15, 37:22. It was also known that decreasing agitation or dissolved oxygen during culturing would result in increases of DHA. MARA-1007, 28:15-17, 27:13-21.

A PHOSITA would have therefore understood and/or found obvious to apply Kralovec’s (or similar) methods to Radianingtyas’s microbial oil to produce a DHA-enriched microbial oil containing at least 90% DHA in triglyceride form. MARA-1003, ¶¶153-154. A PHOSITA would understand that having higher levels of DHA in triglyceride form was desirable for the stability and consumer acceptability reasons discussed above in Section III.B.4[2]. MARA-1003, ¶¶155.

Claim 5

[5] The microbial oil of claim 1, further comprising an arachidonic acid content of the triglyceride fraction of between 0.1% and 1.5% by weight.

Radianingtyas-Kralovec discloses and/or renders obvious [5]. MARA-1003, ¶¶156-161.

Both Radianingtyas and Kralovec disclose microbial oils with ARA content between 0.1% and 1.5% by weight. In Radianingtyas, in Example 13, Radianingtyas discloses that “approximately 80% of all isolates synthesized the omega-6 PUFAs, arachidonic acid (AA)...at concentrations varying between 1 and 18%.” MARA-1007, 96:1-3, 99:29-32; *see also id.*, Fig. 11. A PHOSITA would have understood that the low end of this disclosed range falls within the claimed range. Moreover, Radianingtyas discloses that its microbes can produce a wide range of oils that consistently fall within the claimed range. *See* MARA-1007, 34:4-37:14 (showing ARA ranging from 0.13% to 0.90% as percentage of total fatty acid). Because Radianingtyas discloses that its compositions include triglycerides from “96 to about 100%” of the neutral lipids, which “can be at least 95% by weight of total lipids,” a PHOSITA would have understood that the ARA was likely to be found in triglyceride form. MARA-1007, 32:17-33:5; *see also* MARA-1037, 2908-2909 & tbl.2 (disclosing oil similar to Radianingtyas with 96% triglycerides in the neutral lipids and 0.37% ARA in the triglyceride fraction). Thus, a PHOSITA would have understood that the amount of ARA in triglyceride form would not deviate significantly from the 0.13-0.90% disclosed in Radianingtyas, and therefore would fall within the claimed range of 0.1-1.5%. MARA-1003, ¶¶157-159.

Additionally, Kralovec provides an example showing that after using Kralovec's method for increasing DHA, ARA (i.e. fatty acid 20:4) is present at no more than 1.4% of the glyceride fraction. *See* MARA-1030, 43-44 (tbl.9.1); MARA-1003, ¶160.

As also discussed prior in Section III.B.4[1c], a PHOSITA would have understood that it was desirable to have low levels of ARA in a primarily DHA-containing oil because higher purity oils resulted in more efficient supplementation. MARA-1003, ¶161. Thus, a PHOSITA would have sought out microbial oils containing low amounts of ARA, as taught in Radianingtyas and in Kralovec.

Claim 6

[6] The microbial oil of any one of claims 1 to 5, wherein said microbial oil further comprising an effective amount of at least one added antioxidant to provide oxidative stability.

Radianingtyas-Kralovec discloses and/or renders obvious [6]. MARA-1003, ¶¶162-166.

Radianingtyas teaches that the oil “compositions can contain any antioxidants.” MARA-1007, 37:30, 11:10-13. Radianingtyas also discloses compositions that contain “lipid with antioxidant.” MARA-1007, 40:22-26; *see also id.*, 12:3-7. A PHOSITA would have understood that the addition of an

effective amount of an antioxidant was desirable because it would provide oxidative stability. MARA-1003, ¶¶163-164.

Radianingtyas discloses that “the addition of antioxidants” is utilized to “enhance production of omega-3 fatty acids.” MARA-1007, 12:20-22 (referencing Barclay, MARA-1019). The Barclay patent that Radianingtyas cites describes “adding an antioxidant compound...in order to prevent degradation of the omega-3 HUFAs” such as DHA. MARA-1019, 5:35-40; *see also id.*, 12:45-48, 14:16-17 (confirming antioxidants “protect the fatty acids from oxidation” and “improve their stability”); MARA-1003, ¶¶164-165.

The stabilizing qualities of antioxidants were well known to a PHOSITA; it was noted “that many microbial oils contain relatively large quantities of their own antioxidants,” meaning that those oils were “much more stable than corresponding oils [extracted] from plants and marine animals.” MARA-1010, 204. It was a “standard process” as of 2009 to add antioxidants to microbial oils “to prolong shelf life.” MARA-1038, 3645-46. Indeed, microbial oils are “stabilized by adding antioxidants,” including “ascorbyl palmitate and tocopherols.” MARA-1010, 213. Therefore, the “standard commercial practice” was “to add further antioxidants to the oils in order to assure the customer that all the necessary steps have been taken to ensure complete stability of the oil.” MARA-1010, 204. MARA-1003, ¶166.

Claim 7

[7] A food product composition for animals or humans, comprising the microbial oil of any one of claims 1 to 6.

Radianingtyas-Kralovec discloses and/or renders obvious [7]. MARA-1003, ¶¶167-169.

Radianingtyas states that its “oils can be used directly as a feed or food additive[.]” MARA-1007, 42:22-23; *see also id.*, 12:3-7, 40:20-26, 42:7-9, 43:6-8, 72:4-17.

Claim 8

[8] The food product of claim 7, wherein the food product is an infant formula.

Radianingtyas-Kralovec discloses and/or renders obvious [8]. MARA-1003, ¶¶170-172.

Radianingtyas discloses that the “compositions can be used in food products (e.g., baby milk).” MARA-1007, 13:15-16; *see also id.*, 40:25-26 (“disclosed is an infant formula comprising the composition”), 67:18-19, 79:12-17, claim 38.

Claim 9

[9] The food product of claim 7, wherein the food product is milk, a beverage, a therapeutic drink, a nutritional drink, or a combination thereof.

Radianingtyas-Kralovec discloses and/or renders obvious [9]. MARA-1003, ¶¶173-175.

Radianingtyas discloses that the “compositions can be used in food products (e.g., baby milk).” MARA-1007, 13:15-16; *see also id.*, 72:15-17 (“the foodstuff is...milk...fruit juice, a dry beverage powder...”), 79:11-13, 79:19-21, claim 40.

Claim 10

[10] The food product of claim 7, wherein the food product is an additive for animal or human food.

Radianingtyas-Kralovec discloses and/or renders obvious [10]. MARA-1003, ¶¶176-177.

Radianingtyas discloses that its compounds “are useful as...*food additives*.” MARA-1007, 11:18-21; *see also id.*, 12:3-7, 42:22-25, 43:6-8.

Claim 11

[11] The food product of claim 7, wherein the food product is a nutritional supplement.

Radianingtyas-Kralovec discloses and/or renders obvious [11]. MARA-1003, ¶¶178-179.

Radianingtyas discloses that its compounds “are useful as...*nutraceuticals*.” MARA-1007, 11:18-21; *see also id.*, 43:6-8 (discloses oils can be “used as a *nutritional supplements*[sic] for humans”), 12:3-7, 59:16, 59:21-24.

Claim 12

[12] The food product of claim 7, wherein the food product is an animal feed.

Radianingtyas-Kralovec discloses and/or renders obvious [12]. MARA-1003, ¶¶180-181.

Radianingtyas discloses a “**foodstuff**, supplement, pharmaceutical composition for both human **and animal** (including marine) can comprise the composition (lipid, lipid with antioxidant and antioxidant alone).” MARA-1007, 40:20-26; *see also id.*, 67:18 (“These lipids and antioxidants are targeted for use in **animal feeds**.”), 12:3-7, claim 39.

Claim 13

[13] The animal feed of claim 12, wherein the animal feed is an aquaculture feed.

Radianingtyas-Kralovec discloses and/or renders obvious [13]. MARA-1003, ¶¶182-183.

Radianingtyas discloses a “composition for both human **and animal** (**including marine**) can comprise the composition.” MARA-1007, 40:20-26; *see also id.*, 79:11-18 (“The foodstuff can also be...an **aquaculture feed**.”), claim 39.

Claim 14

[14] The animal feed of claim 12, wherein the animal feed is a domestic animal feed, a zoological animal feed, a work animal feed, a livestock feed, or a combination thereof.

Radianingtyas-Kralovec discloses and/or renders obvious [14]. MARA-1003, ¶¶184-185.

Radianingtyas discloses a “**foodstuff**, supplement, pharmaceutical composition for both human **and animal** (including marine) can comprise the composition[.]” MARA-1007, 40:20-26; *see also id.*, 79:11-18 (“The foodstuff

can also be a fish product, a *companion pet food, a livestock* or an aquaculture *feed.*”), claim 39.

C. GROUND 3: Claims 1-14 are obvious over Bijl in view of Nichols-I and Kralovec

1. Overview of Bijl

Bijl, like the '959 patent, is directed to microbial oils. MARA-1008, 2:30-36, 9:5-7; MARA-1001, 1:27-32, 1:63-2:18, 2:33-52, 10:16-14:24. Bijl also discloses high quality microbial oils sourced from naturally-occurring microorganisms and processes for obtaining quality microbial oils. MARA-1008, 12:22-37, 2:35-3:2; MARA-1003, ¶186.

Bijl's microbial oils contain one or more polyunsaturated fatty acids and a triglyceride content of at least 90 wt.%. MARA-1008, 2:30-33, 5:24-29. The microbial oils of Bijl also can contain additional compounds, such as anti-oxidants, which remain from the sourced microorganisms. *Id.*, 3:9-14. Bijl discloses oils having low diglyceride content and low monoglyceride content. *Id.*, 5:14-19. Bijl's microbial oils are usable in food, nutritional supplements, and cosmetics. *Id.*, 4:13-18; MARA-1003, ¶187.

Bijl also describes processes for obtaining microbial oils. One process involves extracting microbial oil from dried granules. MARA-1008, 6:23-34. Another process involves culturing microorganisms in fermentation broth, pasteurizing the resulting broth or biomass, and then extracting microbial oil from

the biomass. *Id.*, 7:2-11. These processes may be combinable as well. *Id.*, 8:1-6, 28:28-29:19; MARA-1003, ¶188.

Bijl teaches using pasteurization to partially inactivate one or more compound degrading substance(s), such as enzymes (e.g., lipases) that may be present in the biomass or broth. MARA-1008, Abstract, 7:12-30. The pasteurization process removes undesirable substances that can cause degradation of parts of the compound and contributes to obtaining high quality PUFAs. *Id.*, 7:12-30; MARA-1003, ¶189. Bijl teaches that, in particular, “degradation is particularly high when the PUFA is ARA.” MARA-1008, 3:25-27.

Bijl’s processes for obtaining microbial oils utilize less solvent for extracting microbial oils than prior methods and produce higher quality crude oils. MARA-1008, 9:5-15; MARA-1003, ¶190.

2. Overview of Nichols-I

Nichols-I discloses newly-discovered sources of long-chain polyunsaturated fatty acids (“LC-PUFAs”) in microorganisms. Nichols-I describes new strains of single cell organisms that produce high quantities of LC-PUFAs. MARA-1009, 27. Nichols-I discloses that different fatty acids are obtained from different microorganisms: for example, DHA from dinoflagellates and thraustochytrids; and ARA from red algae, thraustochytrids, and fungi. *Id.*, 27 (tbl.1). And Nichols-I also reports on the relative fatty acid concentrations of certain strains of

thraustochytrids and their main omega-3 long-chain polyunsaturated fatty acids (LC-PUFA): DHA and EPA (strain A); DHA and arachidonic (AA) (strains C/H); and DHA (strain O) fatty acids. *Id.*, 27 (tbl.2); MARA-1003, ¶¶191-192. Strain O is “particularly attractive” because it “contains very high levels of DHA (61%).” MARA-1009, 27. Strain O also contains low levels of ARA (0.7%). *Id.*; MARA-1003, ¶193

Nichols-I also discloses uses and benefits of microbially-derived oils. Nichols-I teaches that omega-3 oils are beneficial to human health and are used to treat diseases and in development and protection of the human brain. MARA-1009, 26. Nichols-I further teaches that different omega-3 oils have different health benefits. DHA, for example, decreases the incidence of coronary heart disease. *Id.*; MARA-1003, ¶194.

Traditionally, omega-3 oils were derived from fish. MARA-1009, 26. As Nichols-I describes, however, “there is a need for new sources of these oils to be obtained” because “global wild fish stocks are declining.” *Id.*, 26. So, not only does Nichols-I describe the use of microorganisms as sources of omega-3 oils, it also describes suggestions for creating transgenic plants that contain genes of oil-producing microorganisms, to enable farmers to grow omega-3-producing plants. *Id.*, 28; MARA-1003, ¶195.

3. Overview of Kralovec

See Section III.B.2, *supra*.

4. Combination of Bijl and Nichols-I

It would have been obvious for a PHOSITA to combine the teachings of Bijl, directed to microbial oils and processes of cultivating, processing, and extracting microbial oils from natural sources, with Nichols-I, which teaches using specific beneficial strains of microorganisms (e.g., thraustochytrids). MARA-1003, ¶197. A PHOSITA would have found it obvious to implement Nichols-I's teachings of using a preferred strain of microorganisms (e.g., thraustochytrids of a strain O) as a microbial source for Bijl's extracted microbial oil for at least the following reasons.

First, a PHOSITA would have been motivated to use Nichols-I's preferred microbial strains (e.g., strain O thraustochytrids) as a microbial source for Bijl's extracted microbial oil because doing so "provide[s] an oil of a particularly high quality." MARA-1008, 9:5-7; MARA-1003, ¶198.

Second, a PHOSITA would have been motivated to use Nichols-I's preferred microbial strains as a source for Bijl's extracted microbial oil because "[t]hraustochytrids are...single cell organisms that produce both high oil and LC-PUFA content." MARA-1009, 27; MARA-1003, ¶199.

Third, a PHOSITA would have been motivated to use Nichols-I's preferred

microbial strains as a source for Bijl's extracted oil because these strains were "a highly attractive, renewable and contaminant free, source of omega-3 oils" and "thraustochytrids can be grown in fermenters with an organic carbon source," which provides a renewable and contaminant free microbial source. MARA-1009, 27; MARA-1003, ¶200.

Fourth, a PHOSITA would have been motivated to use Nichols-I's preferred microbial strains as a source for Bijl's extracted oil because "[s]train O is particularly attractive as it contains very high levels of DHA (61%)." MARA-1009, 27; MARA-1003, ¶201. As Nichols-I notes, DHA is "beneficial against various human disorders." MARA-1009, 26; MARA-1003, ¶201. Moreover, as discussed above, there are many known benefits associated with DHA. MARA-1030, 1:16-2:3, 18:10-19:6; *see also* MARA-1010, 99, 182-186.

Fifth, a PHOSITA would have been motivated to use Nichols-I's preferred microbial strains as a source for Bijl's extracted oil because Strain O contained only 0.7% ARA. MARA-1009, 27 (tbl.2); MARA-1003, ¶202. Bijl teaches that "degradation is particularly high when the PUFA is ARA." MARA-1008, 3:25-27. Thus, a PHOSITA would have been motivated to use Strain O, which contained low levels of ARA.

Sixth, a PHOSITA would have been motivated to use Nichols-I's preferred microbial strains as a source for Bijl's extracted oil because doing so

would have amounted to nothing more than the use of a known technology (e.g., identifying a microbial source) to improve similar oils (e.g., extracted microbial oils) in the same way and combining prior art elements according to known methods (e.g., apply Bijl's oil extraction methods) to yield predictable results (e.g., obtain an oil with desirable traits such as high PUFA levels). *KSR*, 550 U.S. at 417; MARA-1003, ¶203; MARA-1010, 38-42, 47-48, 202-17. For these reasons above, a PHOSITA would have found it obvious to combine the teachings of Bijl with the disclosures of Nichols-I to obtain an improved extracted microbial oil.

A PHOSITA would also have a reasonable expectation of success in combining Bijl with Nichols-I. Bijl and Nichols-I both relate to the creation of microbial oils using culturing techniques. MARA-1008, 7:2-11; MARA-1009, 27-28. Both references teach the same sources of those microbial oils: algae, fungi, dinoflagellates, and other diatoms. MARA-1008, 12:22-37; MARA-1009, 27; *see also* MARA-1018, [0569]-[0570] (tbl.3); MARA-1020, 384-385 (tbl.2). And both teach that the desired product is one of high enough quality for use in the human diet, including in infant formula. MARA-1008, 14:23-27; MARA-1009, 27-28. Furthermore, Bijl discloses that its processes are compatible with a wide range of natural sources, including *Thraustochytrium*, which are also disclosed in Nichols-I. MARA-1008, 6:3-11, 13:19-31; MARA-1009, 27; MARA-1003, ¶204.

5. Combination of Bijl, Nichols-I, and Kralovec

Kralovec provides methods for obtaining compositions containing “triglycerides with higher DHA...contents than the starting triglycerides.” MARA-1030, 35:20-32. Like the combination of Radianingtyas and Kralovec described above in Section III.B.3.b, it would have been obvious for a PHOSITA to combine the teachings of Bijl-Nichols-I, directed to microbial oils having high levels of triglycerides (e.g., >97%) with a preferred PUFA (DHA), with Kralovec, directed to methods for modifying an oil composition, to increase the concentration of that PUFA in the microbial oil. MARA-1008, 2:30-33, 4:24-28; MARA-1030, 1:9-11; MARA-1003, ¶¶205-206. Specifically, a PHOSITA would have found it obvious to implement Kralovec’s oil modification techniques (or similar) to Bijl-Nichols-I’s method and extracted microbial oil to increase the amount of DHA for at least the following reasons.

First, a PHOSITA would have been motivated to apply Kralovec’s oil modification techniques to the Bijl-Nichols-I extracted microbial oil to increase its DHA content because “purifying and concentrating PUFA’s [sic] in a triglyceride form is generally desired.” MARA-1030, 2:7-8; MARA-1003, ¶207. It would have been well-known that decreasing the amount of unwanted components in a microbial oil would be desirable because “[p]olyunsaturated fatty acids, such as, for example omega-3 fatty acids, are often derived from marine oils, microbial,

and/or algal oils,” which “typically provide the PUFA in a triglyceride form where other undesired, fatty acids...are present along side a desired PUFA in the triglyceride molecule.” MARA-1030, 2:4-8; MARA-1003, ¶207.

Second, a PHOSITA would have been motivated to apply Kralovec’s oil modification techniques to the Bijl-Nichols-I extracted microbial oil to increase its DHA content because the produced oils include “‘designer’ glycerides” and “often non-naturally occurring, ratios of polyunsaturated fatty acid ester” that provide “triglycerides that have better color and lower levels of trans-isomers” as well as “better sensory properties.” MARA-1030, 35:21-36:2; MARA-1003, ¶208. “Such oils can be incorporated into food products, nutraceuticals, pharmaceutical formulations, and microcapsules.” MARA-1030, 35:21-36:2.

Third, a PHOSITA would have been motivated to apply Kralovec’s oil modification techniques to the Bijl-Nichols-I extracted microbial oil because such combinations reflect nothing more than the use of a known technology (e.g., enzymatic modification) to improve similar oils (e.g., extracted microbial oils) according to known methods (e.g. oil refinement methods) to yield predictable results (e.g., obtain oil with an increased concentration of DHA). *KSR*, 550 U.S. at 417; MARA-1003, ¶209.

A PHOSITA would have expected success in applying Kralovec’s techniques to increase the concentration of the preferred PUFA (i.e., DHA) in the

microbial oil because Bijl contemplates that its invention “can be subjected to one or more further refining steps.” MARA-1008, 9:20-22; MARA-1003, ¶210. Thus, a PHOSITA would have looked to refine the Bijl-Nichols-I oils in accordance with Bijl-Nichols-I’s teachings by looking to Kralovec. MARA-1003, ¶210.

Moreover, a PHOSITA would have expected success in using Kralovec’s method techniques for increasing the concentration of the preferred PUFA (i.e., DHA), particularly in the context of an extracted microbial oil, given that Bijl-Nichols-I and Kralovec teach that their oils are microbial/algal in origin and so have similar characteristics. MARA-1008, 13:19-22; MARA-1030, 2:28-29; MARA-1003, ¶211. Bijl and Kralovec both acknowledge their oils are specific to containing omega-3 PUFAs, and even more specifically DHA. MARA-1008, 6:3-5, 7:18-19; MARA-1030, 19:7-12. Furthermore, both Bijl-Nichols-I and Kralovec acknowledge similar uses for their oils, such as human nutritional uses. MARA-1008, 9:30-36; MARA-1030, 35:31-36:2; MARA-1003, ¶212.

6. Analysis

Claim 1

[1pre] A microbial oil comprising

Bijl-Nichols-I-Kralovec discloses and/or renders obvious [1pre]. MARA-1003, ¶¶213-215.

Bijl discloses a “pure and stable microbial oil” which comprises “at least one polyunsaturated fatty acid (PUFA), which has a triglyceride content of greater than

90%.” MARA-1008, 1:8-11; 2:30-33. Bijl discloses obtaining “microbially derived” oils by “extracting, isolating or recovering the compound from the microbial biomass.” *Id.*, 3:3-5, 7:10-11. And Bijl notes that “PUFA (oil) which has been extracted can be used” with or without further refining. *Id.*, 9:20-22. Nichols-I and Kralovec similarly disclose microbial oils. *See* MARA-1009, 26-27; MARA-1030, 6:28-7:2; MARA-1003, ¶214.

As described above in Section III.B.4[1pre], a PHOSITA would also have been familiar with microbial oils as of the Critical Date.

[1a] a triglyceride fraction of at least 70% by weight,

Bijl-Nichols-I-Kralovec discloses and/or renders obvious [1a]. MARA-1003, ¶¶216-219.

Bijl discloses a microbial oil “which has a triglyceride content of greater than 90%.” MARA-1008, 2:30-33. Bijl discloses a triglyceride content greater than 95 wt.% and optionally higher than 97 wt.%. *Id.*, 4:24-28.

Similarly, Kralovec discloses oils that “have a high TG (triglyceride) content,” for example, “the oil can comprise greater than or equal to about 60%, 65%, 70%, 75%, or 80% TG by weight of the total composition.” MARA-1030, 37:22-24; *see also id.*, 36, tbl.5 (disclosing “TG content” of “60-80%” “after the disclosed hydrolysis and esterification”); MARA-1003, ¶218.

Indeed, triglyceride-rich oils were well known to a PHOSITA prior to the

Critical Date. Consistent with the teachings in Bijl and Kralovec, other references (e.g., Singh) also disclosed triglyceride-rich oils. MARA-1018, [0294] (“oil comprising at least 75% or 85% triacylglycerols...said triacylglycerols comprising the LC-PUFA”); MARA-1003, ¶219.

[1b] wherein the docosaehaenoic acid content of the triglyceride fraction is at least 45% by weight,

Bijl-Nichols-I-Kralovec discloses and/or renders obvious [1b]. MARA-1003, ¶¶220-227.

A PHOSITA would have applied the teachings of using a preferred microbial strain (e.g., *thraustochytrid* strain O), as taught by Nichols-I, to Bijl’s oil to yield an improved oil composition having higher amounts of DHA. MARA-1003, ¶221. A PHOSITA would have found it obvious that the DHA content of the triglyceride fraction is at least 45 wt.% in the proposed combination because Nichols-I’s preferred strain O of *Thraustochytrium*, when cultured, produces an oil composition with greater than 60 wt.% DHA. MARA-1009, 27, tbl.2; MARA-1003, ¶221. Specifically, Nichols-I discloses that *Thraustochytrium* strain O contains “very high levels of DHA (61%).” MARA-1009, 27, tbl.2; MARA-1018, [0571]; MARA-1020, 384-385, tbl.2. Consistent with Nichols-I’s disclosure, other prior art references indicated that many microbial strains (e.g., strains in the *Thraustochytrium* family) contained DHA in amounts greater than 45 wt.%, and even greater than 60 wt.%. MARA-1032, 27-31, tbl.2.5 (discloses 67.2, 65.6, 67.8,

63.7, 64.3, 62.4 and other percentages DHA); MARA-1015, [0107]-[0108], [0113]-[0114], [0016], Fig. 3; MARA-1019, tbls.3-4 (showing multitude of strains with >45% DHA (C22:6w3)). Komazawa is another example that discloses a *Thraustochytrium* strain (LFF1 strain) that contains DHA components ranging from 62% to 84% in triglyceride form. MARA-1015, [0113]-[0114], [0016], Fig. 3.

A PHOSITA would have understood since the majority of Bijl's microbial oil is made up of triglycerides (e.g., > 97%), that the majority of the DHA (61%) in Bijl-Nichols-I is present in the triglyceride form. MARA-1003, ¶224. In fact, Bijl discloses that DHA is a preferred PUFA associated with the triglycerides present in its oil. MARA-1008, 6:3-5, 7:18-19.

A PHOSITA would have therefore understood and/or found obvious to apply Kralovec's (or similar) methods to the Bijl-Nichols-I microbial oil to produce a DHA-enriched microbial oil containing at least 45 wt.% DHA, or higher, such as at least 60 wt.% DHA or at least 80 wt.% DHA in triglyceride form. MARA-1003, ¶¶225-227. That in turn discloses or renders obvious [1b]. *Id.* ***[1c] and wherein the oil comprises 1.5% by weight or less of arachidonic acid.***

Bijl-Nichols-I-Kralovec discloses and/or renders obvious [1c]. MARA-1003, ¶¶228-233.

Element [1c] is an optional negative limitation, for which prior art disclosure

is not necessary to meet the claim element. “[A] reference need not state a feature’s absence in order to disclose a negative limitation.” *AC Techs., S.A. v. Amazon.com, Inc.*, 912 F.3d 1358, 1367 (Fed. Cir. 2019). In other words, an oil containing no ARA meets this limitation. Indeed, during prosecution the Examiner determined that the initial claim, which recited “less than 5% heptadecanoic acid,” could be amended around “by adding to claim 51 the limitation that the amount of heptadecanoic acid is between 0.1% and 5% by weight (i.e., not zero).” MARA-1002, 158-159. Because applicants retained the “less than language,” it means that art that does not disclose that the oil contains any ARA reads on the patent.

However, to the extent a non-zero amount of ARA that is less than 1.5 wt.% is required, Bijl-Nichols-I-Kralovec discloses and/or renders obvious this limitation. Nichols-I discloses that Strain O contains 0.7% ARA total fatty acids. MARA-1009, 27. And Kralovec teaches that in an embodiment, after processing, ARA is present at no more than 1.4% of the glyceride fraction. MARA-1030, 43-44, tbl.9.1; *see also* MARA-1019, tbl.3 (indicating 72.7% DHA and 0% ARA). That in turn discloses or renders obvious [1c]. MARA-1003, ¶¶231-232.

Additionally, as discussed in Section III.B.4[1c], a PHOSITA would have understood that it was desirable to have low levels of ARA in a primarily DHA-containing oil because higher purity oils result in more efficient supplementation. MARA-1003, ¶233. Thus, a PHOSITA would have sought out microbial oils

containing low amounts of ARA, as taught in Nichols-I and in Kralovec.

Claim 2

[2] The microbial oil of claim 1, wherein said docosahexaenoic acid content of the triglyceride fraction is at least 60% by weight.

See Section III.C.6[1b], *supra*; MARA-1003, ¶234.

Claim 3

[3] The microbial oil of claim 1, wherein said docosahexaenoic acid content of the triglyceride fraction is at least 80% by weight.

The Bijl-Nichols-I-Kralovec combination discloses and/or renders obvious [3]. MARA-1003, ¶¶235-238.

As described above, compositions having a DHA content of the triglyceride fraction that is at least 80% or at least 90% by weight were also known to a PHOSITA based on the prior art that was available before the Critical Date. MARA-1003, ¶¶235-237; Section III.C.6[1b], *supra*.

To the extent the DHA content in triglyceride form in is determined to be less than 80% (or 90%), a PHOSITA would have been further motivated to apply Kralovec's oil modification techniques (or similar) to increase DHA content, as discussed above in Sections III.C.4 and III.C.5. MARA-1003, ¶238. In doing so, Kralovec discloses its methods can be used to produce "concentrated oils with triglycerides containing higher proportions of polyunsaturated fatty acid esters than the starting glycerides," such as "oils that comprise *greater than or equal to* about...80% DHA by weight of the total composition." MARA-1030, 35:20-27,

36:12-15. Such oils would “also have a high TG (triglyceride) content” and the method would “produce triglycerides of fatty acids.” MARA-1030, 35:27-30, 37:22. The end result would be “an oil having higher levels of a PUFA...than the starting oil composition.” MARA-1030, 5:24-32.

Claim 4

[4] The microbial oil of claim 1, wherein said docosahexaenoic acid content of the triglyceride fraction is at least 90% by weight.

See §III.B.6[3], *supra*; MARA-1003, ¶239.

Claim 5

[5] The microbial oil of claim 1, further comprising an arachidonic acid content of the triglyceride fraction of between 0.1% and 1.5% by weight.

The Bijl-Nichols-I-Kralovec combination discloses and/or renders obvious [5]. MARA-1003, ¶¶240-242.

As discussed above, both Kralovec and Nichols-I disclose microbial oils with ARA content between 0.1% and 1.5% by weight. *See* Section III.C.6[1c], *supra*. Because Bijl discloses that its compositions include triglycerides in over 97% of the total composition, a PHOSITA would have understood that the ARA was likely to be found in triglyceride form. MARA-1003, ¶¶241.

As discussed above in Section III.B.4[1c], a PHOSITA would have understood that it was desirable to have low levels of ARA in a primarily DHA-containing oil because higher purity oils resulted in more efficient supplementation. Thus, a PHOSITA would have sought out microbial oils

containing low amounts of ARA, as taught in Nichols-I and in Kralovec.

Claim 6

[6] The microbial oil of any one of claims 1 to 5, wherein said microbial oil further comprising an effective amount of at least one added antioxidant to provide oxidative stability.

Bijl-Nichols-I-Kralovec discloses and/or renders obvious [6]. MARA-1003, ¶243.

Bijl teaches that antioxidants, such as tocopherol or ascorbyl palmitate, can be added to compositions. MARA-1008, 26:16-18. Its composition may also contain antioxidants. MARA-1008, 3:37-4:1. MARA-1003, ¶243.

Claim 7

[7] A food product composition for animals or humans, comprising the microbial oil of any one of claims 1 to 6.

Bijl-Nichols-I-Kralovec discloses and/or renders obvious [7]. MARA-1003, ¶244.

Bijl teaches that the oil of its invention can “be used in *foods, foods stuffs* or *food compositions* or serve as a nutritional supplement, for *humans* as well as for *animals*.” MARA-1008, 4:13-15; *see also id.*, 4:17-18, 9:28-10:8, 14:23-27, 29:2-25, cls. 33-36. Nichols-I also teaches that the “oils are being *incorporated into food products*.” MARA-1009, 27; MARA-1003, ¶244.

Claim 8

[8] The food product of claim 7, wherein the food product is an infant formula.

Bijl-Nichols-I-Kralovec discloses and/or renders obvious [8]. MARA-1003, ¶¶245.

Bijl teaches that the oil of its invention “are particularly suitable for inclusion in *infant formula*.” MARA-1008, 9:37-10:1; *see also id.*, 4:13-18, 9:28-10:8, 14:23-27, 29:20-25, cls. 33-36. Nichols-I also teaches that oils “are being *incorporated into food products* and *in infant formula*.” MARA-1009, 27; *see also id.*, tbl.1 (identifying thraustochytrid-derived DHA as good for infant formula). MARA-1003, ¶245.

Claim 9

[9] The food product of claim 7, wherein the food product is milk, a beverage, a therapeutic drink, a nutritional drink, or a combination thereof.

Bijl-Nichols-I-Kralovec discloses and/or renders obvious [9]. MARA-1003, ¶246.

Bijl teaches that the oil of its invention can used in “*milk, health drinks*, and bread,” as well as *infant formula*. MARA-1008, 9:28-10:8; *see also id.*, 4:13-18, 14:23-27, 29:20-25, cls. 33-36. Nichols-I also teaches that oils “are being *incorporated into food products* and *in infant formula*[.]” MARA-1009, 27; *see also id.*, tbl.1. MARA-1003, ¶246.

Claim 10

[10] The food product of claim 7, wherein the food product is an additive for animal or human food.

Bijl-Nichols-I-Kralovec discloses and/or renders obvious [10]. MARA-1003, ¶247.

Bijl teaches that the oil of its invention can “***be used in foods***, foods stuffs or food compositions or serve as a nutritional supplement, ***for humans as well as for animals***.” MARA-1008, 4:13-15; *see also id.*, 4:17-18, 9:28-10:8, 14:23-27, 29:20-25, cls. 33-36. Nichols-I also teaches that oils “are being ***incorporated into food products***.” MARA-1009, 27; *see also id.*, tbl.1. MARA-1003, ¶247.

Claim 11

[11] The food product of claim 7, wherein the food product is a nutritional supplement.

Bijl-Nichols-I-Kralovec discloses and/or renders obvious [11]. MARA-1003, ¶248.

Bijl teaches that the oil of its invention can “***be used in foods***, foods stuffs or food compositions or serve ***as a nutritional supplement, for humans as well as for animals***.” MARA-1008, 4:13-15; *see also id.*, 4:17-18, 9:28-10:8, 14:23-27, 29:20-25, cls. 33-36. Table 1 of Nichols-I also identifies thraustochytrid-derived DHA as good for “[a]quaculture, ***health supplements***, [and] infant formula.” MARA-1009, 27, tbl.1; *see also id.*, 27. MARA-1003, ¶248.

Claim 12

[12] The food product of claim 7, wherein the food product is an animal feed.

Bijl-Nichols-I-Kralovec discloses and/or renders obvious [12]. MARA-1003, ¶249.

Bijl teaches that the oil of its invention can “***be used in foods***, foods stuffs or food compositions or serve as a nutritional supplement, ***for humans as well as for animals***.” MARA-1008, 4:13-15; *see also id.*, 4:17-18 (“granular particles or granules may find use as a food or ***feed composition or supplement***”), 9:28-10:8, 14:23-27, 29:20-25, cls. 33-36. Nichols-I also teaches that oils “are being ***incorporated into food products***.” MARA-1009, 27; *see also id.*, tbl.1 (identifying thraustochytrid-derived DHA as good for aquaculture); MARA-1003, ¶249.

Claim 13

[13] The animal feed of claim 12, wherein the animal feed is an aquaculture feed.

Bijl-Nichols-I-Kralovec discloses and/or renders obvious [13]. MARA-1003, ¶250.

Nichols-I teaches that “[t]hese unique microorganisms can be used ***in aquaculture*** to supply essential LC-PUFA to ***live feeds used for rearing larvae***, and as components in ***aquaculture feeds*** (e.g. pellets) used for raising juvenile and adult finfish and crustaceans (prawns and lobsters).” MARA-1009, 27; *see also id.*, tbl.1 (identifying thraustochytrid-derived DHA as good for aquaculture);

MARA-1003, ¶250.

Claim 14

[14] The animal feed of claim 12, wherein the animal feed is a domestic animal feed, a zoological animal feed, a work animal feed, a livestock feed, or a combination thereof.

Bijl-Nichols-I-Kralovec discloses and/or renders obvious [14]. MARA-1003, ¶251.

Bijl teaches that the oil of its invention can “***be used in foods***, foods stuffs or food compositions or serve as a nutritional supplement, ***for humans as well as for animals.***” MARA-1008, 4:13-15; *see also id.*, 4:17-18 (“granular particles or granules may find use as a food or ***feed composition or supplement***”), 9:28-10:8, 14:23-27, 29:20-25, cls. 33-36. Nichols-I teaches using microorganisms in aquaculture in “***live feeds used for rearing larvae***, and...***aquaculture feeds*** (e.g. pellets) used for raising juvenile and adult finfish and crustaceans (prawns and lobsters).” MARA-1009, 27; *see also id.*, tbl.1; MARA-1003, ¶251.

D. GROUND 4: Claims 1-4, 6-14 are obvious over Bijl in view of Komazawa

1. Overview of Bijl

See Section III.C.1, *supra*.

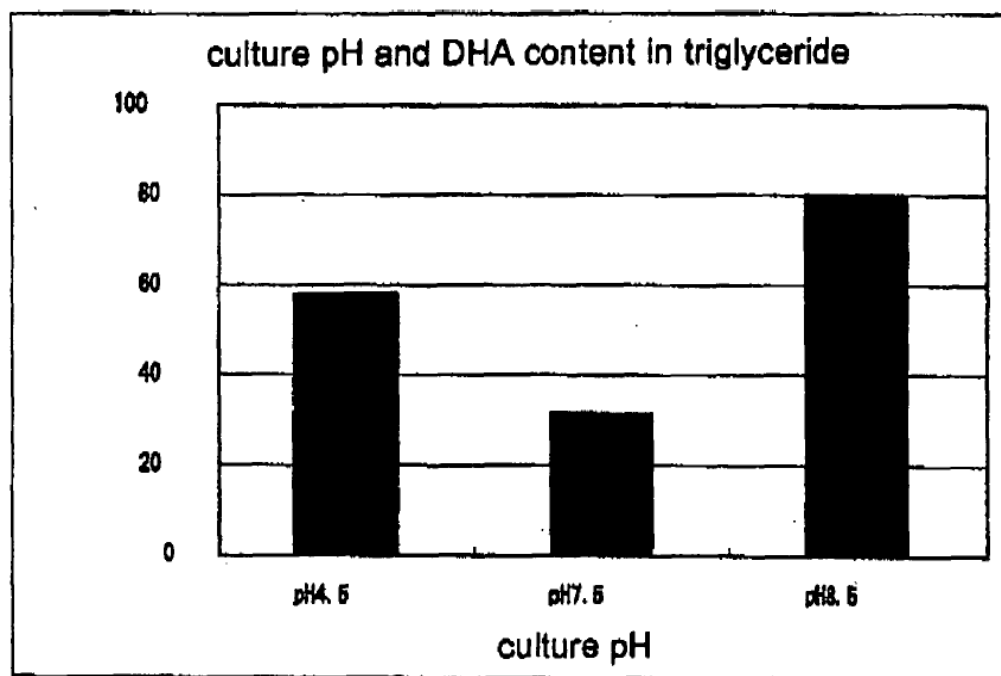
2. Overview of Komazawa

Komazawa “relates to a novel microorganism having an ability of producing docosahexaenoic acid (DHA) and the use of said microorganism.” MARA-1015,

[0001]. In particular, Komazawa teaches “culturing the *Thraustochytrium* strain having an ability of producing docosahexaenoic acid in a medium, and collecting the docosahexaenoic acid-containing fat and oil from the culture product.”

MARA-1015, [0012]; MARA-1003, ¶253.

Komazawa teaches that “to promote the production of docosahexaenoic acid, a docosahexaenoic acid precursor can be added to a medium.” MARA-1015, [0044]. Komazawa discloses that the “DHA component is around 40% when culturing was carried out at pH 7.5, but DHA component becomes a high content of 80% or more, when culturing was carried out at pH 8.5.” *Id.*, [0116], Fig. 3; MARA-1003, ¶254.



MARA-1015, FIG. 3.

Komazawa teaches increased omega-3 fatty acid (DHA) concentrations in microbial oils. Furthermore, Komazawa also teaches that “when docosahexaenoic acid is used in the field of medicines or the like, it is necessary that docosahexaenoic acid is separated and purified from docosahexaenoic acid-containing fat and oil” but “a variety of polyunsaturated fatty acids having structures similar to that of docosahexaenoic acid are contained, and thus, separation and purification are difficult”—a problem that Komazawa sought to solve. MARA-1015, [0003]; MARA-1003, ¶255. A PHOSITA would have recognized that Komazawa discloses highly purified DHA-containing oils that would be understood to contain little or no ARA. MARA-1003, ¶255. To the extent any ARA was present, a PHOSITA would have understood it to be below the limit of detection. MARA-1003, ¶255.

3. Combination of Bijl and Komazawa

It would have been obvious for a PHOSITA to combine the teachings of Bijl, directed to microbial oils and processes of cultivating, processing, and extracting microbial oils from natural sources, with Komazawa, which teaches using specific beneficial strains of microorganisms (e.g., thraustochytrids) cultured under certain conditions to increase DHA. MARA-1003, ¶256. A PHOSITA would have found it obvious to implement Komazawa’s teachings of using a preferred strain of microorganisms (e.g., thraustochytrids of a strain LFF1) as a

microbial source for Bijl's extracted microbial oil for at least the following reasons.

First, a PHOSITA would have been motivated to use Komazawa's preferred microbial strains (e.g., strain LFF1 *thraustochytrids*) as a microbial source for Bijl's extracted microbial oil because doing so "provide[s] an oil of a particularly high quality." MARA-1008, 9:5-7; MARA-1003, ¶257.

Second, a PHOSITA would have been motivated to use Komazawa's preferred microbial strains as a source for Bijl's extracted microbial oil because the *Thraustochytrium* strain of Komazawa "can be easily cultured, and can produce fat and oil which contain a large amount of DHA." MARA-1015, [0009]; MARA-1003, ¶258.

Third, a PHOSITA would have been motivated to use Komazawa's preferred microbial strains as a source for Bijl's extracted oil because when the LFF1 strain is used, the obtained "fat and oil is advantageous for concentration and separation of docosahexaenoic acid" because it "contains substantially no fatty acid having physiological activities similar or agonistic to that of docosahexaenoic acid." MARA-1015, [0058], MARA-1003, ¶259.

As Komazawa notes, DHA is "present specifically in the brain or retina of an animal" and "plays a major physiological role in those organs, and also has physiological activities such as an anti-inflammatory effect or an effect of lowering

blood cholesterol level.” MARA-1015, [0002]; MARA-1003, ¶260. Moreover, as discussed above, there are many known benefits associated with DHA. MARA-1030, 1:16-2:3, 18:10-19:6; *see also* MARA-1010, 99, 182-186. Thus, Komazawa notes that “application thereof is convenient in the fields of functional foods or medicines, and utilization thereof is particularly convenient in the production of behenic acid which is used for photographic photosensitive materials.” MARA-1015, [0058], MARA-1003, ¶260.

Fifth, a PHOSITA would have been motivated to use Komazawa’s preferred microbial strains as a source for Bijl’s extracted oil because Komazawa’s LFF1 strain contained no measurable amount of ARA. MARA-1015, [0112], tbl.1; MARA-1003, ¶261. To the extent ARA was present in Komazawa’s oil, a PHOSITA would have understood it to be below the limit of detection for the gas chromatography method used, meaning a level of less than 1%, and likely less than <0.1% ARA, as Dr. Curtis describes. MARA-1003, ¶261. As discussed above, it was desirable for a DHA-containing oil to have high purity, and a PHOSITA would have considered ARA to be a contaminant. Thus, a PHOSITA would have been motivated to use the LFF1 strain, which contained low levels of ARA.

Sixth, a PHOSITA would have been motivated to use Komazawa’s preferred microbial strain as a source for Bijl’s extracted oil because doing so would have amounted to nothing more than the use of a known technology (e.g.,

identifying a microbial source) to improve similar oils (e.g., extracted microbial oils) in the same way and combining prior art elements according to known methods (e.g., apply Bijl's oil extraction methods) to yield predictable results (e.g., obtain an oil with desirable traits such as high PUFA levels). *KSR*, 550 U.S. at 417; MARA-1003, ¶262; MARA-1010, 38-42, 47-48, 202-17. For the reasons above, a PHOSITA would have found it obvious to combine the teachings of Bijl with the disclosures of Komazawa to obtain an improved extracted microbial oil.

A PHOSITA would also have a reasonable expectation of success in combining Bijl with Komazawa. Bijl and Komazawa both relate to the creation of microbial oils using culturing techniques. MARA-1008, 7:2-11; MARA-1015, [0012], [0116], FIG. 3. Both references teach the same sources of those microbial oils: algae, fungi, dinoflagellates, and other diatoms. MARA-1008, 12:22-37; MARA-1015, [0004]; *see also* MARA-1018, [0569]-[0570], tbl.3; MARA-1020, 384-385, tbl.2. Furthermore, Bijl discloses that its processes are compatible with a wide range of natural sources, including *Thraustochytrium*, which are also disclosed in Komazawa. MARA-1008, 6:3-11; 13:19-31; MARA-1015, [0004], [0009]-[0011]. And both teach that the desired product is one of high enough quality for use in the human diet, including in infant formula. MARA-1008, 14:23-27; MARA-1015, [0060]; MARA-1003, ¶¶263.

4. Analysis

Claim 1

[1pre] A microbial oil comprising

Bijl-Komazawa discloses and/or renders obvious [1pre]. MARA-1003, ¶¶264-267.

Bijl discloses [1pre]. *See* Section III.C.6[1pre], *supra*. Additionally, Komazawa teaches the production of DHA-containing oil from a microbe—*Thraustochytrium*—and therefore, it discloses a microbial oil as well. MARA-1003, ¶¶265-266.

As described above in Section III.B.4[1pre], a PHOSITA would also have been familiar with microbial oils as of the Critical Date.

[1a] a triglyceride fraction of at least 70% by weight,

Bijl-Komazawa discloses and/or renders obvious [1a]. MARA-1003, ¶¶268-272.

Bijl discloses [1a]. *See* Section III.C.6[1a], *supra*. Additionally, as Dr. Curtis explains, a PHOSITA would also understand Komazawa to contain predominantly triglycerides because Komazawa teaches the use of lipase for triglyceride-specific oils. MARA-1015, [0021], [0055], MARA-1022, 185; MARA-1003, ¶270.

A PHOSITA would also have understood Komazawa's disclosures as referring to predominantly triglyceride compositions. Komazawa describes its

invention as “fat and oil,” which to a PHOSITA predominantly refers to triglycerides (or neutral lipids). MARA-1003, ¶271; *see* MARA-1015, [0146]. If Komazawa were referring to non-triglyceride-form lipids, Komazawa would have otherwise used a term like “total lipid” to refer to multiple lipid classes. MARA-1003, ¶271.

Indeed, triglyceride-rich oils were well known to a PHOSITA prior to the Critical Date. MARA-1018, [0294] (“oil comprising at least 75% or 85% triacylglycerols...said triacylglycerols comprising the LC-PUFA”); MARA-1030, 35:20-27, 36:12-15, 37:22; MARA-1003, ¶272.

[1b] wherein the docosahexaenoic acid content of the triglyceride fraction is at least 45% by weight,

Bijl-Komazawa discloses and/or renders obvious [1b]. MARA-1003, ¶¶273-275.

A PHOSITA would have applied the teachings of using a preferred microbial strain (e.g., *thraustochytrid* strain LFF1), as taught by Komazawa, to Bijl’s oil to yield an improved oil composition having higher amounts of a desired PUFA (e.g., DHA). MARA-1003, ¶274. A PHOSITA would have found it obvious that the DHA content of the triglyceride fraction is at least 45 wt.% in the proposed combination because Komazawa’s preferred strain LFF1 of *Thraustochytrium*, when cultured, produces an oil composition with greater than 60 wt.% DHA. Additionally, a PHOSITA would generally have understood that

Thraustochytrium microbes would have produced oil that was “preferably 50% by weight or more” DHA. MARA-1015, [0058], [0108]; MARA-1009, 27, tbl.2; MARA-1032, 27-31, tbl.2.5 (discloses 67.2, 65.6, 67.8, 63.7, 64.3, 62.4 and other percentages of DHA). Moreover, Komazawa discloses that its culturing method can be used to produce oils having a “DHA component in the triglycerides” with “a high content of 80% or more,” based on its culturing conditions. MARA-1015, [0116], FIG. 3. Because 80% DHA in the triglycerides is greater than 45%, Bijl-Komazawa teaches and/or renders obvious [1b]. MARA-1003, ¶¶274-275.

[1c] and wherein the oil comprises 1.5% by weight or less of arachidonic acid.

Bijl-Komazawa discloses and/or renders obvious [1c]. MARA-1003, ¶¶276-279. As described above, element [1c] is an optional negative limitation, for which prior art disclosure is not necessary to meet the claim element.

Komazawa teaches an example of a “fatty acid composition of the extracted lipid” that contains no detectable amount of ARA. MARA-1015, [0112], tbl.1 (showing 100% oils with no ARA). To the extent any ARA is present in Komazawa’s oil, it is below the limit of detection, which is lower than 1.5% based on the data in Table 1. Komazawa therefore discloses and/or renders obvious [1c]. MARA-1003, ¶278.

As discussed previously (Section III.B.4[1c]), a PHOSITA would have understood that low levels of ARA were desirable in a primarily DHA-containing

oil because higher purity oils resulted in more efficient supplementation. MARA-1003, ¶279. Thus, a PHOSITA would have sought out microbial oils containing low amounts of ARA.

Claim 2

[2] The microbial oil of claim 1, wherein said docosahexaenoic acid content of the triglyceride fraction is at least 60% by weight.

See Section III.D.2[1b], *supra*; MARA-1003, ¶280.

Claim 3

[3] The microbial oil of claim 1, wherein said docosahexaenoic acid content of the triglyceride fraction is at least 80% by weight.

See Section III.D.2[1b], *supra*; MARA-1003, ¶281.

Claim 4

[4] The microbial oil of claim 1, wherein said docosahexaenoic acid content of the triglyceride fraction is at least 90% by weight.

See Section III.D.2[1b], *supra*; MARA-1003, ¶282.

Claim 6

[6] The microbial oil of any one of claims 1 to 5, wherein said microbial oil further comprising an effective amount of at least one added antioxidant to provide oxidative stability.

Bijl-Komazawa discloses and/or renders obvious [6]. See Section III.C.6[6], *supra*; MARA-1003, ¶283.

Claim 7

[7] A food product composition for animals or humans, comprising the microbial oil of any one of claims 1 to 6.

Bijl-Komazawa discloses and/or renders obvious [7]. MARA-1003, ¶¶284-

285.

Bijl discloses [7]. *See* Section III.C.6[7], *supra*. Komazawa's oils can likewise "be added to various foods and drinks, feed or bait." MARA-1015, [0060]; MARA-1003, ¶285.

Claim 8

[8] The food product of claim 7, wherein the food product is an infant formula.

Bijl-Komazawa discloses and/or renders obvious [8]. MARA-1003, ¶¶286-287.

Bijl discloses [8]. *See* Section III.C.6[8], *supra*. Komazawa's oils can also be added to "modified *milk for infants or premature babies...baby foods*." MARA-1015, [0060]; MARA-1003, ¶287.

Claim 9

[9] The food product of claim 7, wherein the food product is milk, a beverage, a therapeutic drink, a nutritional drink, or a combination thereof.

Bijl-Komazawa discloses and/or renders obvious [9]. MARA-1003, ¶¶288-289.

Bijl discloses [9]. *See* Section III.C.6[9], *supra*. Komazawa's oils can also "be added to various foods and *drinks*, feed or bait. *Examples of such foods include nutritional supplementary foods*, modified *milk* for infants or premature babies." MARA-1015, [0060]; MARA-1003, ¶289.

Claim 10

[10] The food product of claim 7, wherein the food product is an additive for animal or human food.

Bijl-Komazawa discloses and/or renders obvious [10]. MARA-1003, ¶¶290-291.

Bijl discloses [10]. *See* Section III.C.6[10], *supra*. Komazawa's oils can also "***be added to various*** foods and drinks, ***feed*** or bait." MARA-1015, [0060]; MARA-1003, ¶291.

Claim 11

[11] The food product of claim 7, wherein the food product is a nutritional supplement.

Bijl-Komazawa discloses and/or renders obvious [11]. MARA-1003, ¶¶292-293.

Bijl discloses [11]. *See* Section III.C.6[11], *supra*. Komazawa's oils can also "be added to various foods and drinks, feed or bait....***includ[ing] nutritional supplementary foods.***" MARA-1015, [0060]; MARA-1003, ¶293.

Claim 12

[12] The food product of claim 7, wherein the food product is an animal feed.

Bijl-Komazawa discloses and/or renders obvious [10]. MARA-1003, ¶¶294-295.

Bijl discloses [12]. *See* Section III.C.6[12], *supra*. Additionally, Komazawa's oils can "***be added to various...feed*** or bait." MARA-1015, [0060].

Komazawa's oil can also be used in "*livestock feeds*." MARA-1015, [0060];
MARA-1003, ¶295.

Claim 13

[13] The animal feed of claim 12, wherein the animal feed is an aquaculture feed.

Bijl-Komazawa discloses and/or renders obvious [13]. MARA-1003, ¶296.

Komazawa's oil can be used in "*feed for pisciculture*." MARA-1015,
[0060]. Komazawa's oil may be "*provided as bait for the aquafarming of
seafood*." MARA-1015, [0060]; MARA-1003, ¶296.

Claim 14

[14] The animal feed of claim 12, wherein the animal feed is a domestic animal feed, a zoological animal feed, a work animal feed, a livestock feed, or a combination thereof.

Bijl-Komazawa discloses and/or renders obvious [14]. MARA-1003, ¶¶297-
298.

Bijl and Komazawa each disclose [14]. See Sections III.C.6[14],
III.D.4[12]-[13], *supra*; MARA-1003, ¶¶297-298.

IV. DISCRETION SHOULD NOT PRECLUDE INSTITUTION

The Board should not exercise its discretion to deny institution under 35
U.S.C. § 325(d) because the two-part framework set forth in *Advanced Bionics,
LLC v. MED-El Elektromedizinische Geräte GmbH* is not satisfied. IPR2019-
01469, Paper 6 (PTAB, Feb. 13, 2020).

The first prong of *Advanced Bionics* asks whether the art or arguments presented in the Petition are the same or substantially the same as those previously presented to the Office. *Id.*, 7-8. This inquiry is less probative, however, when art is buried among hundreds of references on multiple pages of an information disclosure statement (IDS). *Shenzhen Zhiyi Tech. Co. v. iRobot Corp.*, IPR2017-02137, Paper 9, 9-10 (P.T.A.B. Apr. 2, 2018) (declining discretion to deny institution because references not relied upon but instead only “included in the approximately fifteen pages of cited references”).

Here, the previously presented art includes Komazawa and Radianingtyas’s United States publication counterparts (disclosed during the parent ’363 patent prosecution) and Bijl (disclosed during the parent ’465 patent prosecution). Each was disclosed in an IDS in their respective prosecutions. Notably, however, Komazawa and Radianingtyas were among over 140 other cited references. And also notable is that none of Komazawa, Radianingtyas, or Bijl were cited in a rejection or discussed substantively during prosecution of any of the ’959 family patents.

Patent Owner may argue that the remaining art presented in this Petition is substantially the same art or presents the same arguments as those presented in prosecution. Petitioner respectfully disagrees. Nichols-I and Kralovec were not before the Examiner; neither was cited during prosecution; and both fully disclose

background teachings that were not discussed by the Examiner during prosecution. For example, the art cited by the Examiner during prosecution of the '959 patent, Fichtali, did not disclose low or non-existent quantities of ARA. In fact, the Examiner never considered arguments that any art disclosed low or non-existent quantities of ARA; thus, the patent was improperly allowed.

As to the second prong of *Advanced Bionics*, that inquiry asks “whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims.” Paper 6, 8. Factors (c), (e), and (f) inform this inquiry. *Id.*, 10-11. Thus, the Board inquires “(c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection...(e) whether petitioner has pointed out sufficiently how the examiner erred in its evaluation of the asserted prior art; and (f) the extent to which additional evidence and facts presented in the petition warrant reconsideration of the prior art or arguments.” *Id.*, 9, n.10.

Regarding factor (c), none of Petitioner’s art was cited by, discussed by, or formed the basis of a rejection by, the Examiner. When art cited in a petition was not applied during prosecution, the Board should not decline to institute. *See Navistar, Inc. v. Fatigue Fracture Tech., LLC*, IPR2018-00853, Paper 13 at 17 (PTAB Sept. 12, 2018) (“Under [factors] (c), (d), and (f)...the fact that [references] were of record, but not applied in any rejection by the Examiner...provides little

impetus for us to exercise our discretion to deny institution under Section 325(d).”).

Regarding factors (e) and (f), the Petition highlights that the Examiner did not further consider prior art after Applicant amended its claims.

For example, the Petition highlights that the art cited in this Petition discloses elements directly responsive to claim amendments. The Examiner allowed the patent after patentee amended its claims to recite a low or non-existent quantity of ARA, instead of heptadecanoic acid. The Examiner, however, should have looked for other art because that amendment materially changed the scope of the claim. As Applicants noted, Fichtali—the only reference cited—disclosed high quantities of ARA. But no rejection to any other art disclosing low or non-existent quantities of ARA followed.

Regarding ARA, the Examiner’s failure to consider any of Radianingtyas, Kralovec, Komazawa, Bijl, or Nichols-I is dispositive. Radianingtyas, Kralovec, and Nichols-I each disclose microbial oils with low ARA values below the claimed 1.5%. And Bijl and Komazawa do not disclose ARA values at all, meaning they nonetheless read on at least claim 1. Thus, each is directly responsive to the amendment which resulted in issuance of the patent. But the Examiner did not make any rejections following this amendment. The Board should therefore decline to exercise its discretion under Section 325(d).

V. CONCLUSION

The Challenged Claims are unpatentable. MARA-1003, ¶¶1-300. Mara authorizes charging of fees to Deposit Account 06-1050.

VI. MANDATORY NOTICES UNDER 37 C.F.R. §42.8(a)(1)

A. Real Party-In-Interest Under 37 C.F.R. §42.8(b)(1)

Mara Renewables Corporation and Algal Omega 3 Ltd. are real parties-in-interest.

B. Related Matters Under 37 C.F.R. §42.8(b)(2)

Mara is not aware of any other judicial or administrative matter that would affect, or be affected by, a decision in this matter.

An IPR was previously filed by Petitioner against a different patent assigned to DSM, U.S. Pat. No. 10,392,578. (*See* IPR2023-01167, filed on July 14, 2023.)

C. Lead And Back-Up Counsel Under 37 C.F.R. §42.8(b)(3)

Mara provides the following designation of counsel.

Lead Counsel	Backup counsel
Gwilym J. Attwell, Reg. No. 45,449 Fish & Richardson P.C. 60 South Sixth Street Suite 3200 Minneapolis, MN 55402 Tel: 202-783-5070 Fax: 877-769-7945 Email: IPR55973-0004IP1@fr.com	Grace Kim, Reg. No. 71,977 Casey M. Kraning, <i>pro hac vice</i> to be filed Fish & Richardson P.C. 60 South Sixth Street Suite 3200 Minneapolis, MN 55402 Tel: 202-783-5070 Fax: 877-769-7945 PTABInbound@fr.com

D. Service Information

Please address all correspondence and service to the address listed above.

Petitioner consents to electronic service by email at IPR55973-0004IP1@fr.com

(referencing No. 55973-0004IP1).

Respectfully submitted,

Dated 8/22/2023

/Grace J. Kim/

Gwilym J. Attwell, Reg. No. 45,449

Grace Kim, Reg. No. 71,977

Casey M. Kraning, *pro hac vice forthcoming*

Fish & Richardson P.C.

60 South Sixth Street

Suite 3200

Minneapolis, MN 55402

T: 202-783-5070

F: 877-769-7945

(Control Number IPR2023-01342) *Attorneys for Petitioner*

CERTIFICATION UNDER 37 CFR § 42.24

Under the provisions of 37 CFR § 42.24(d), the undersigned hereby certifies that the word count for the foregoing Petition for *Inter partes* Review totals 13,896 words, which is less than the 14,000 allowed under 37 CFR § 42.24.

Dated 8/22/2023

/Grace J. Kim/

Gwilym J. Attwell, Reg. No. 45,449

Grace Kim, Reg. No. 71,977

Casey M. Kraning, *pro hac vice forthcoming*
Fish & Richardson P.C.

60 South Sixth Street

Suite 3200

Minneapolis, MN 55402

T: 202-783-5070

F: 877-769-7945

Attorneys for Petitioner

CERTIFICATE OF SERVICE

Pursuant to 37 CFR §§ 42.6(e)(4)(i) *et seq.* and 42.105(b), the undersigned certifies that on August 22, 2023, a complete and entire copy of this Petition for *Inter partes* Review, Power of Attorney, and all supporting exhibits were provided via Federal Express, to the Patent Owner by serving the correspondence address of record as follows:

DSM North America Inc.
Patent Department
6480 Dobbin Road
Columbia, MD 21045
UNITED STATES

/Michael Stanwyck/
Michael Stanwyck
Fish & Richardson P.C.
60 South Sixth Street, Suite 3200
Minneapolis, MN 55402
202-783-5070