

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent of: Stephen Cherinko et al.
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Title: EXTRACTION OF LIPID FROM CELLS AND PRODUCTS
THEREFROM

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**PETITION FOR *INTER PARTES* REVIEW OF UNITED STATES PATENT
NO. 10,392,578 PURSUANT TO 35 U.S.C. §§ 311–319, 37 C.F.R. § 42**

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EXHIBITS

MARA-1001	U.S. Patent No. 10,392,578 to Cherinko et al. (“the ’578 patent”)
MARA-1002	Excerpts from the Prosecution History of the ’578 patent (“the Prosecution History”)
MARA-1003	Declaration of Dr. Jonathan Curtis
MARA-1004	Curriculum Vitae of Dr. Jonathan Curtis
MARA-1005	U.S. Pat. App. Pub. No. 2005/0220958 to Schaap et al. (“Schaap”)
MARA-1006	U.S. Pat. App. Pub. No. 2009/0118525 to Wang (“Wang”)
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 (2d Ed. May 1, 2010, Cohen & Ratledge, eds.)
MARA-1011	P.K. Bajpai et al., <i>Optimization of Production of Docosahexaenoic Acid (DHA) by Thraustochytrium aureum ATCC 34304</i> , 68:7 JAOCS 509 (1991)
MARA-1012	Anita N. Jakobsen et al., <i>Accumulation of docosahexaenoic acid-rich lipid in thraustochytrid Aurantiochytrium sp. strain T66: effects of N and P starvation and O₂ limitation</i> , 80 Appl. Microbiol. Biotechnol. 297 (2008)

MARA-1013	U.S. Pat. App. Pub. No. 2007/0141222 to Binder et al. ("Binder")
MARA-1014	U.S. Pat. App. Pub. No. 2010/0298435 to ABRIL et al. ("Abril")
MARA-1015	U.S. Pat. App. Pub. No. 2004/0161831 to Komazawa et al. ("Komazawa")
MARA-1016	U.S. Pat. No. 8,148,559 to Walker et al. ("Walker")
MARA-1017	U.S. Pat. No. 8,207,363 to Apt et al. ("Apt")
MARA-1018	US Pat. App. Pub. No. 2005/0273885 to Singh et al. ("Singh")
MARA-1019	U.S. Pat. App. Pub. No. 2006/0094089 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	R.D. Bowles et al., <i>Long-chain n-3 polyunsaturated fatty acid production by members of the marine protistan group the thraustochytrids: screening of isolates and optimisation of</i>

docosahexaenoic acid production, J. Biotechnol. 70:193–202
(1999)

- MARA-1027 Edwin N. Frankel, *Lipid Oxidation*, The Oily Press (2005)
- MARA-1028 J. Huang et al., *Profile of Polyunsaturated Fatty Acids Produced by Thraustochytrium sp. KK17-3*. JAOCS, Vol. 78:6 (2001)
- MARA-1029 Willis A. Gortner, *An Evaluation of Micromethods for Phospholipid*, J. Biol. Chem., 159:97-100 (June 1945)
- MARA-1030 WO 2009/040676 to Kralovec et al. (“Kralovec”)
- MARA-1031 T. Yaguchi et al., *Production of High Yields of Docosahexaenoic Acid by Schizochytrium sp. Strain SR21*, 74:11 JAOCS 1431 (1997)
- MARA-1032 Thomas Eric Lewis, *Characterisation and application of Australian thraustochytrids*, Doctoral Thesis, University of Tasmania (June 2001)

LISTING OF CHALLENGED CLAIMS

Claim	Identifier	Claim Language
1	[1pre]	An extracted microbial lipid comprising
	[1a]	a triglyceride fraction of at least 70% by weight of the lipid fraction,
	[1b]	wherein the docosahexaenoic acid content of the triglyceride fraction is at least 50% by weight,
	[1c]	wherein the docosapentaenoic acid n-6 content of the triglyceride fraction is from at least 0.5% by weight to 6% by weight, and
	[1d]	wherein the oil has an anisidine value of 0.5 to 26, and
	[1e]	wherein the lipid has less than 5% by weight of an organic solvent.
2	[2pre]	An extracted microbial lipid comprising
	[2a]	a triglyceride fraction of at least 70% by weight of the lipid fraction,
	[2b]	wherein the docosahexaenoic acid content of the triglyceride fraction is at least 40% by weight,
	[2c]	wherein the docosapentaenoic acid n-6 content of the triglyceride fraction is from at least 0.5% by weight to 6% by weight,
	[2d]	wherein the ratio of docosahexaenoic acid to docosapentaenoic acid n-6 is greater than 6:1, and
	[2e]	wherein the oil has an anisidine value of 0.5 to 26, and
	[2f]	wherein the lipid has less than 5% by weight of an organic solvent.

Claim	Identifier	Claim Language
3	[3pre]	An extracted microbial lipid comprising
	[3a]	a triglyceride fraction of at least 70% by weight of the lipid fraction
	[3b]	wherein the docosahexaenoic acid content of the triglyceride fraction is at least 60% by weight and
	[3c]	wherein the oil has an anisidine value of 0.5 to 26, and
	[3d]	wherein the lipid has less than 5% by weight of an organic solvent.
4	[4]	The extracted microbial lipid of claim 1, wherein the oil has a peroxide value of 5 or less.
5	[5]	The extracted microbial lipid of claim 1, wherein the oil has a phosphorus content of 100 ppm or less.
6	[6]	The extracted microbial lipid of claim 1, wherein the lipid is a crude oil.
7	[7]	A process for obtaining a lipid, the process comprising refining a crude lipid of claim 6.

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 1-7 (“the Challenged Claims”) of U.S. Patent No. 10,392,578 (“the ’578 patent”). 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 ’578 patent is available for IPR. Mara has not filed any civil litigation challenging the validity of the ’578 patent nor has any litigation been filed against Mara accusing it of patent infringement. 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, ¶¶1-306.

Ground	’578 patent Claims	Basis for §103 Rejection
1	3	Schaap and Kralovec
2	1-7	Schaap and Komazawa
3	1-7	Bijl, Nichols-I, and Schaap
4	3	Radianingtyas and Wang

Each applied reference pre-dates U.S. provisional application 61/350,363, filed on June 1, 2010, the earliest filed application to which the '578 patent claims priority. Petitioner does not take a position as to whether the '578 patent is entitled to the priority date of June 1, 2010 (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.¹

Reference		Date Published	Section
Schaap	US 2005/0220958	October 6, 2005	§102(b)
Kralovec	WO 2009/040676	April 2, 2009	§102(b)
Komazawa	US 2004/0161831	Aug. 19, 2004	§102(b)
Bijl	WO 1997/037032	October 9, 1997	§102(b)

¹ Schaap (the US counterpart to WO 2004/001021) and Bijl appear on the face of the patent, but neither was cited in a rejection or discussed substantively during prosecution.

Reference		Date Published	Section
Nichols-I ²	<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)	§102(b)
Wang	US 2009/0118525	August 9, 2007	§102(b)
Radianingtyas	WO 2008/129358	October 30, 2008	§102(b)

C. Claim Construction under 37 C.F.R. §§42.104(b)(3)

A claim subject to IPR “shall be construed using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b), including construing the claim in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent.” 37 C.F.R. §42.100(b). For purposes of this proceeding only, Mara submits a construction for the term “the oil” below. All remaining terms should be given their plain and ordinary meaning.

² Nichols-I is a printed publication that was publicly available no later than 2004.

See MARA-1021, ¶¶7-10.

1. “THE OIL,” CLAIMS 1-7

The claim phrase “the oil” should be construed to mean “the extracted microbial lipid” in claims 1-7.³ MARA-1003, ¶¶17-19. The claims of the ’578 patent support this construction. For example, each of independent claims 1-3 recite “wherein the oil has an anisidine value of 0.5 to 26.”⁴ MARA-1001, cls. 1-3. But the phrase “the oil” has no antecedent basis in any of those claims. *Id.* Petitioner’s interpretation would resolve the lack of antecedent basis present in claims 1-7.

The specification supports Petitioner’s interpretation that “lipid” and “oil” can be used interchangeably. Under “DEFINITIONS,” the ’578 patent states “As used herein, ‘lipid’ or ‘oil’ refers to one or more fatty acids.” MARA-1001, 12:31-38.

II. SUMMARY OF THE ’578 PATENT

A. Brief Description

Generally, the ’578 patent describes a process to lyse a cell and obtain a lipid by separation, as well as properties of the obtained lipids. MARA-1001, Abstract. “Known methods can be used to culture a thraustochytrid of the invention, to

³ While claims 6 and 7 do not recite “the oil,” they both depend from claim 1.

⁴ Emphasis has been added in this document unless otherwise noted.

isolate a biomass from the culture, and to analyze the fatty acid profile of oils extracted from the biomass.” *Id.*, 34:16-19.

The lipid obtained from the process of the ’578 patent possesses certain physical properties. The lipids are described as having little “fishy” aftertaste and “a lower anisidine value, lower peroxide value, lower phosphorus content and/or a higher extraction yield than if extraction was performed using a solvent[.]” *Id.*, 32:4-6, 32:52-56. Additionally, lipids claimed by the invention contain varying levels of docosahexaenoic acid (DHA), *id.*, 4:4-8, and docosapentaenoic acid (DPA n-6), *id.*, 4:8-10, such that the triglyceride fraction of the lipid is at least 70 wt.% of the total lipid, *id.*, 5:46-67. Further, lipids claimed by the ’578 patent have anisidine values of less than 26, *id.*, 3:53-55, and less than 5 wt.% organic solvent, *id.*, 6:54-55. MARa-1003, ¶¶49-50

B. Summary of the Prosecution History of the ’578 Patent

The ’578 patent issued on August 27, 2019. *See* MARA-1001; MARA-1003 ¶52. The initial application included 62 claims, of which claims 52-58 eventually issued in modified form. *See* MARA-1002, 155-156; MARA-1003, ¶53. Claims 52-54 matured into granted claims 1-3. MARA-1003, 155-156. Each of claims 52-54 resembled the as-issued claims, but lacked the recitation of a lower anisidine value (0.5) and “less than 5% organic solvent.” *Compare id. with* MARA-1001, cls. 1-3. These claims, after amendments to remove multiple dependencies, were

allowed without substantive prosecution on August 21, 2014, three years into prosecution. MARA-1002, 230-234.

During prosecution, the Examiner rejected claims 52 and 54-57 over Dueppen, U.S. Pub. 2005/0115897, and claim 53 over Dueppen in view of Metz, U.S. Pub. 2008/0148433. *Id.*, 266-268. Claim 58 was rejected as anticipated by Fichtali, U.S. Pub. 2008/0107791. *Id.*, 269. In response, Applicants amended claims 52-54 to add the element “wherein the lipid has less than 5% by weight of an organic solvent.” *Id.*, 286. In doing so, Applicants attempted to distinguish Dueppen by arguing that Dueppen teaches a suspension of DPA n-6 and DHA in a solid fraction commingled with acetone polar solvents, arguing that Dueppen teaches away from a nearly solvent-free solution. *Id.*, 289-292. And Applicants argued that “Metz does not cure the deficiencies of Dueppen.” *Id.*, 292-293; MARA-1003, ¶¶54-55.

Furthermore, during prosecution, the Examiner rejected claims 52-54 for obviousness-type double patenting, noting that the claims “recite ingredients in the oil that need not be present,” and rejected claims 52-58 as obvious over both Elswyk (U.S. Pub. 2003/0060509) and Apt (U.S. Pat. No. 8,207,363). MARA-1002, 1018, 1021-1022. Specifically, the Examiner noted that the Elswyk and Apt references did not “disclose that the oil contains any organic solvent or the anisidine value.” *Id.*, 1022; MARA-1003, ¶56. In response, Applicant agreed and

amended its claims to recite an anisidine value within the range of 0.5 to 25.

MARA-1002, 1068, 1073; *see id.*, 1067-1074; MARA-1003, ¶57. The '578 patent then issued without comment from the Examiner. MARA-1002, 1076-1080.

C. The Effective Priority Date of the Claims of the '578 patent

The '578 patent issued from U.S. Application No. 13/151,014, filed June 1, 2011. The '578 patent claims priority to three provisional applications, the earliest of which was filed on June 1, 2010.

Claims 1-3 of the '578 patent are independent claims. Claims 4-7 depend directly or indirectly from claim 1. All claims have an effective filing date no earlier than June 1, 2010.⁵

D. Level of Ordinary Skill in the Art

A person of ordinary skill in the art relating to the subject matter of the '578 patent as of June 1, 2010 (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, ¶60. Alternatively, the person could

⁵ Petitioner does not concede that there is adequate Section 112 support to sustain this priority date and reserves the right to challenge the priority date.

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, ¶¶38-48. 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.*

III. THE CHALLENGED CLAIMS ARE UNPATENTABLE

This request describes how the prior art discloses each of the elements of the Challenged Claims, thereby rendering claims 1-7 of the '578 patent unpatentable.

A. GROUND 1: Claim 3 is obvious over Schaap and Kralovec

1. Schaap

Schaap, like the '578 patent, is directed to processes for obtaining microbial oils with heightened quality that minimize industrial processing costs. MARA-1001, 1:48-61, 2:8-12; MARA-1005, [0013]. Schaap recognizes that microbial oils naturally occur in a variety of microorganisms and comprise high levels of polyunsaturated fatty acids ("PUFAs"). MARA-1001, 13:16-16:3; MARA-1005, [0002]. Schaap discloses pasteurizing microorganisms, after which PUFAs or microbial oils are extracted for use. MARA-1005, [0001]; MARA-1003, ¶63.

In addition to disclosing processes to obtain microbial oils, Schaap also discloses the properties of the microbial oils prepared by using such processes.

Schaap teaches obtaining a microbial oil “compris[ing] at least 10, 35, 40, or 45% or more of a desired PUFA” and containing “at least 90%” triglycerides, by using a pasteurization process followed by “extracting and/or isolating a PUFA from the pasteurised cells.” MARA-1005, [0041]-[0042], [0056], [0055]. Further, the resulting microbial oils will comprise PUFAs, including a preferred PUFA, e.g., DHA. *Id.* [0045]-[0053]. Schaap teaches that the end product will have an anisidine value between 5 and 25. *Id.*, [0082]-[0083]. The end product can be “extracted from the cells by using a solvent, such as supercritical carbon dioxide, hexane or isopropanol,” (*id.*, [0057]), and extraction is followed by evaporation of the solvent, (*id.*, [0112]). *See also* MARA-1003, ¶64.

Schaap thus discloses, as does the '578 patent, an oil that contains primarily triglycerides, DHA, and has a low concentration of solvent and a low anisidine value. MARA-1005, [0013], [0045]-[0053], [0083]-[0085], [0112]; MARA-1001, 2:16-21, 5:46-53, MARA-1003, ¶65.

2. Kralovec

Kralovec relates to methods for modifying oil concentrations by concentrating polyunsaturated fatty acids. Kralovec recognizes that omega-3 fatty acids like DHA have “well established” beneficial effects, such as reduction of “cardiovascular and heart disease risk.” 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, ¶66.

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 customizable 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, ¶67.

Kralovec’s method employs three steps: hydrolysis, separation, and esterification. *Id.*, 9:8-10, 11:15-28, 12:13-16, 13:27-30. This method provides compositions containing “triglycerides with higher DHA...contents than the starting triglycerides.” *Id.*, 35:20-32. MARA-1003, ¶68.

3. Schaap-Kralovec Combination

1) DHA as the preferred PUFA

As discussed above (§III.A.1, *supra*), Schaap teaches a “microbial oil may comprise at least...45% or more of a desired PUFA,” in which the “[p]referred PUFAs include[s]...docosohexaenoic acid (DHA).” MARA-1005, [0053], [0056].

Based on Schaap's disclosure and other prior art, it would have been obvious for a PHOSITA to have sought microbial oils having high levels of DHA as the preferred PUFA before the Critical Date. MARA-1005, [0056]; MARA-1030, 1:9-11; MARA-1003, ¶69. A PHOSITA would have been motivated to obtain DHA as the preferred PUFA in Schaap's extracted microbial oil for multiple reasons.

First, a PHOSITA would have been motivated to seek DHA as the preferred PUFA in Schaap's extracted microbial oil because there were many recognized health benefits associated with DHA. MARA-1003, ¶70. For example, DHA was known to reduce "cardiovascular and heart disease risk," "prevent[] and/or treat[]...inflammation, neurogenerative diseases, and cognitive development," and was associated with "a strong insulin permeability enhancement effect." MARA-1030, 1:16-2:3, 18:10-19:2; *see also* MARA-1010, 117.

Second, a PHOSITA would have been motivated to seek DHA as the preferred PUFA in Schaap's microbial oil because DHA is an omega-3 fatty acid, known to be "vital to everyday life and function." MARA-1030, 1:13-14; MARA-1003, ¶71. For example, omega-3 fatty acids "exhibit proven effects on lowering serum triglyceride levels," "cardioprotective benefits," and "have strong connection to diabetes." MARA-1030, 18:8-12, 1:13-2:3.

Specifically, a PHOSITA would have been motivated to obtain DHA as the preferred PUFA in Schaap'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, ¶72. For example, Schaap discloses DHA as one of the three “suitable” n-3 PUFAs (DHA, ALA, and EPA). MARA-1005, [0045]-[0053]; MARA-1003, ¶¶72-73.

A PHOSITA would have expected to be successful in pursuing DHA as the preferred PUFA in an extracted oil because Schaap identifies DHA as a preferred PUFA. MARA-1005, [0053]; MARA-1003, ¶73. Moreover, a PHOSITA would have expected success in pursuing DHA as the preferred PUFA particularly in the context of an extracted microbial oil given that it was already known that certain strains of microbials contained “very high levels of DHA (61%).” MARA-1009, 27; MARA-1003, ¶73.

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

Kralovec provides methods for obtaining compositions containing “triglycerides with higher DHA...contents than the starting triglycerides.” §III.A.2, *supra*; MARA-1030, 35:20-32. It would have been obvious for a PHOSITA to combine the teachings of Schaap, directed to microbial oils having high levels of triglycerides (e.g., >98%) 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-1005, [0056], MARA-1030, 1:9-11; MARA-1003, ¶74. Specifically, a PHOSITA would have found it

obvious to implement Kralovec's oil modification techniques to Schaap'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 Schaap'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, ¶75. 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, ¶75.

Second, a PHOSITA would have been motivated to apply Kralovec's oil modification techniques to Schaap'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, ¶76. "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 Schaap’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 DHA). *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007); MARA-1003, ¶77.

A PHOSITA would have expected to be successful in applying Kralovec’s techniques to increase the concentration of the preferred PUFA (i.e., DHA) in the microbial oil because Schaap contemplates that its invention “can be subjected to one or more refining steps.” MARA-1005, [0065]; MARA-1003, ¶78. Moreover, a PHOSITA would have naturally considered Kralovec’s methods for modifying the oil because Schaap discloses that “the oil can be subjected to...free fatty acid removal” or to apply “winterisation...to remove saturated triglycerides[.]” MARA-1005, [0065]; MARA-1003, ¶78. Kralovec discloses that its methods remove saturated free fatty acids. MARA-1030, 2:20-24. Kralovec also discloses that its methods are a “substitute for a winterization process.” MARA-1030, 13:1-4. Thus, a PHOSITA would have looked to refine Schaap’s oils in accordance with Schaap’s teachings by looking to Kralovec. MARA-1003, ¶79.

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 Schaap and Kralovec teach that their oils are microbial/algal in origin and so have similar characteristics. MARA-1005, [0063]; MARA-1030, 2:28-29; MARA-1003, ¶79. Both acknowledge their oils are specific to containing omega-3 PUFAs, and even more specifically DHA. MARA-1005, [0045]-[0046]; MARA-1030, 19:7-12. Furthermore, both Schaap and Kralovec acknowledge similar uses for their oils, such as human nutritional uses. Schaap, for example, teaches that its resultant oil can be used for "nutritional purposes" and "be added to (human) foods." MARA-1005, [0066]. Kralovec too discloses that its oils "can be incorporated into food products." MARA-1030, 35:31-36:2.

4. Analysis

Claim 3

[3pre]

Schaap-Kralovec discloses and/or renders obvious [3pre]. MARA-1003, ¶¶80-81. Schaap generally describes an extraction process for obtaining microbial oil from microbial cells. MARA-1005, [0062]-[0063]. Specifically, Schaap describes "a PUFA-containing microbial oil." *Id.*, cl. 5, [0063]. The PUFA can be "a single PUFA or two or more different PUFAs." *Id.*, [0044]. Schaap describes that the "PUFA may be produced by the cells...such as a microbial cell," including

“Mortierella, Phycomyces, Blakeslea, Aspergillus, Thraustochytrium, Pythium or Entomophthora.” Id., [0054].

Schaap teaches an “extracted microbial lipid.” MARA-1003, ¶¶80-81. For example, Schaap describes that its “microbial oil may be extracted from the cells.” MARA-1005, [0001], [0095], [0085] (Table). Also consistent with disclosure provided in the ’578 specification,⁶ a PHOSITA would have understood Schaap’s “microbial oil...extracted from the cells” to mean microbial *lipids* extracted from microbial cells. *Id.*, [0057]; MARA-1003, ¶¶80-81.

[3a]

Schaap-Kralovec discloses and/or renders obvious [3a]. MARA-1003, ¶¶82-91.

The ’578 patent does not define the term “lipid fraction.” Ordinarily, a PHOSITA would interpret “lipid fraction” to mean solely the lipid portion of the extracted composition, excluding non-lipid components. MARA-1003, ¶83. That is because lipid extracts may generally comprise lipid components and residual solvents. MARA-1010, 180-181; MARA-1003, ¶83. The residual solvent is not

⁶ As discussed in Section I.C.1, “lipid” and “oil” can be used interchangeably. *See* MARA-1001, 12:31-38 (“‘lipid’ or ‘oil’ refers to one or more fatty acids”).

part of the “lipid fraction,” and so the “lipid fraction” is less than 100 wt.% of the entire composition. MARA-1003, ¶83.

The ’578 patent, however, claims further (in [3d]) that “the lipid has less than 5% by weight of an organic solvent.” But the ’578 patent uses the terms “the oil” and “the lipid” interchangeably, so an ambiguity arises. Either the “less than 5% by weight of an organic solvent” element is part of “the oil/the lipid” but not part of the “lipid fraction” because solvent is not a lipid, or the “less than 5% by weight of an organic solvent” element is part of the “lipid fraction” because it is found in “the oil” and therefore is part of the “extracted microbial lipid” as a whole. MARA-1003, ¶84. Under either interpretation, Schaap and/or Kralovec disclose and/or render obvious [3a].

To the extent that “lipid fraction” is interpreted as being synonymous with the extracted microbial lipid—i.e., the “lipid fraction” is 100 wt.% of the extracted microbial lipid—then Schaap discloses or renders obvious the claimed element under such a meaning. Under such an interpretation, triglycerides would constitute at least 70 wt.% of the total composition *and* of the “lipid fraction.” MARA-1003, ¶¶85-86.

Schaap discloses a composition containing triglycerides in an amount of at least 70 wt.% percent of the total composition. For example, Schaap teaches that “optimally at least 70%” of the fatty acids are triglycerides, and may be higher,

“such as at least 85%, preferably at least 90%, optimally at least 95% or 98% of the oil” are triglycerides. MARA-1005, [0055], [0056]. Schaap also “prefer[s] that most of the PUFA is in the form of triglycerides.” *Id.*, [0055].

In the combination, Kralovec’s post-extraction methods would further increase the triglyceride fraction of the extracted microbial lipid composition. The method “produce[s] triglycerides of fatty acids,” which result in oils with “a high TG (triglyceride) content.” MARA-1030, 35:27-28, 37:22. From Schaap’s starting oil, which has at least 70% triglycerides, applying Kralovec’s methods would further increase the amount and concentration of triglycerides. MARA-1030, 5:24-26; MARA-1003, ¶88.

If a reference reads on [3a] under the above narrower interpretation that “lipid fraction” is synonymous with the extracted microbial lipid, then that same reference also meets the claim requirements under the second interpretation, which assumes that a “lipid fraction” comprises solely of the lipid portions of the extracted microbial lipid. MARA-1003, ¶¶89-91. Thus, for efficiency, the remainder of this petition will address the first interpretation of “lipid fraction” to demonstrate that the ground references teach or render obvious the Challenged Claims.

[3b]

Schaap-Kralovec discloses and/or renders obvious [3b]. MARA-1003,

¶¶92-100.

Schaap teaches that its “microbial oil may comprise at least...45% or more of a desired PUFA.” MARA-1005, [0056]; MARA-1003, ¶97. Schaap also teaches a PUFA-containing microbial oil that includes “a single PUFA or two or more different PUFAs,” including DHA. MARA-1005, [0044]. Indeed, Schaap recognizes DHA as a “preferred” PUFA. *Id.*, [0045]-[0046], [0053], cl. 10. As explained above (§III.A.3.1, *supra*), DHA was well-known and sought after for its many benefits and therefore would have been sought after as a preferred PUFA. MARA-1003, ¶97; *see also* MARA-1010, 117.

Moreover, a PHOSITA would have understood that *Thraustochytrium* microbes, such as those disclosed in Schaap, would have produced oil that was “preferably 50% by weight or more” DHA. MARA-1015, [0058], [0108]; MARA-1009, 29; MARA-1032, 27-31 (Table 2.5 discloses 67.2, 65.6, 67.8, 63.7, 64.3, 62.4 and other percentages DHA). Accordingly, a PHOSITA would have understood from Schaap’s disclosure that its composition comprises at least 50 wt.% DHA since there *is* “45% or more” of DHA, a “[p]referred” PUFA. MARA-1005, [0053]. *See In re Peterson*, 315 F.3d 1325, 1329-30 (Fed. Cir. 2003) (“[E]ven a slight overlap in range establishes a *prima facie* case of obviousness.”).

Additionally, a PHOSITA would have understood that in the Schaap microbial oil, most of the PUFAs would be in triglyceride form. MARA-1003,

¶¶93-95. Schaap’s disclosures confirm this to be the case: “Preferably, the microbial oil has a triglyceride content of from 90 to 100%” which is “optimally at least 95% or 98% of the oil.” MARA-1005, [0055]-[0056]. A PHOSITA would have understood since the majority of Schaap microbial oil is made up of triglycerides (e.g., up to 100%), it would have been understood that majority of the PUFAs in Schaap are present in the triglyceride form. MARA-1003, ¶¶93-95.

Even if some fatty acids were not present in triglyceride form, and instead present as free fatty acids, salts, fatty acid esters, phospholipids, or as mono- or diglycerides, Schaap discloses that those alternative forms are not present in significant quantities. MARA-1005, [0085] (Table). Phospholipids, for example, preferably are present in very low quantities. *Id.* (0.05% phospholipids). Free fatty acids are also less than 0.08% in certain cases. *Id.*, *see also* [0089]. To a PHOSITA, this means that most of the fatty acids—and therefore DHA—are in triglyceride form in the lipid fraction. MARA-1003, ¶¶93-95.

In the combination, a PHOSITA would have been motivated to apply Kralovec’s oil modification techniques to Schaap’s extracted microbial oil to increase its DHA content. §III.A.3, *supra*; MARA-1003, ¶99. 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 Schaap’s microbial oil to produce a concentration of DHA in the triglyceride form of the microbial oil such that the resulting oil contains at least 50 wt.% DHA, or higher, such as at least 60 wt.% DHA in the triglyceride fraction. MARA-1003, ¶100. As discussed above, Schaap discloses that its oils are derived from microbial sources, including those from *Thraustochytrium*. MARA-1005, [0045]-[0046]. Furthermore, it was well known to a PHOSITA, based on the prior art available before the Critical Date, that particular microbial strains (e.g., strain O thraustochytrid) contained a high level of DHA (e.g., 61% or higher). MARA-1009, 27; MARA-1003, ¶98; *see also* MARA-1032, 27-31 (Table 2.5 discloses 67.2, 65.6, 67.8, 63.7, 64.3, 62.4 and other percentages DHA). It would have therefore been obvious and/or understood that such strains were a desirable microbial source from which to produce Schaap’s extracted microbial oil. MARA-1003, ¶98. Additionally, it would have been obvious that applying Kralovec’s techniques to microbial oil derived from a high-

DHA containing strain (and extracted according to Schaap's process) would produce oils having levels of DHA significantly above the starting amount (e.g., 61%) in the triglyceride fraction since Schaap's microbial oil generally contains a high triglyceride content (up to 100%). MARA-1018, [0571]; MARA-1020, 384-385, Table 2; MARA-1003, ¶¶98-100.

[3c]

Schaap-Kralovec discloses and/or renders obvious [3c]. MARA-1003, ¶¶101-102.

As discussed above (§I.C.1), the term "the oil" means "extracted microbial lipid" in the Challenged Claims because the specification and claims treat the terms "oil" and "lipid" as equivalent terms. Thus, for [3c], the requirement that "the oil" has an anisidine value of 0.5 to 26 is equivalent to requiring that an extracted microbial lipid has an anisidine value of 0.5 to 26. MARA-1003, ¶¶101-102.

A PHOSITA would have understood from Schaap's disclosure that the combination would be expected to have anisidine values between 0.5 and 26. MARA-1005, [0082]-[0083]. Schaap discloses that preferable anisidine values of its oils range from 5 to 25. *Id.* Experimental results from Schaap demonstrate that its oils have anisidine values ranging from 5 to 15. *Id.* And Figure 5 also demonstrates that Schaap's exemplary extracted oils have anisidine values under

25. *Id.*, Fig. 5, [0011], [0132].

[3d]

Schaap-Kralovec discloses and/or renders obvious [3d]. MARA-1003, ¶¶101-110.

Element [3d] is optional, 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). The ’578 patent specification describes the presence of less than 5% by weight of an organic solvent as an “optional” element because it specifically describes that “the lipid optionally contains less than 5% by weight or volume of an organic solvent.” MARA-1001, 2:21-22; *see also*, 2:49-63. In other words, a lipid containing no organic solvent meets this limitation. Indeed, during prosecution the Examiner determined that the claims “recite ingredients in the oil that need not be present,” meaning that art that “does not disclose that the oil contains any organic solvent” reads on the patent. MARA-1002, 1018, 1021-1022. Applicants acquiesced to that interpretation, agreeing that references that “do[] not disclose that the oil contains any organic solvent” read on the claim. MARA-1002, 1073. Thus, Applicants confirmed that the element is a negative, optional element. *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1570 (Fed. Cir. 1988) (“A statement in a patent that something is in the prior art is binding on the

applicant and patentee for determinations of anticipation and obviousness.”).

However, to the extent a non-zero amount of organic solvent that is less than 5 wt.% is required, Schaap discloses and/or renders obvious this. For example, Schaap discloses a crude oil obtained by extraction using a solvent (e.g., hexane) having no more than 2000 ppm of that solvent in its composition. MARA-1005, [0057], [0063]-[0065], [0085] (Table), [0088]; MARA-1003, ¶¶104-105. A PHOSITA would have understood that 2000 ppm equates to 0.2 wt.% organic solvent. MARA-1003, ¶104. Accordingly, a PHOSITA would have understood that Schaap’s crude oil contains no more than 0.2 wt.% (i.e., 2000 ppm) of the solvent in the extracted microbial lipid composition, and therefore the organic solvent would constitute less than 5 wt.% of the composition. MARA-1003, ¶¶104-105.

Further, a PHOSITA would have understood that residual organic solvents from extracting microbial oils were not desirable and would seek to limit or remove them from a raw or unrefined extracted oil composition (e.g., crude oil). MARA-1003 ¶¶106-110; MARA-1016, 2:24-34 (“ecological problems”), *id.* (“toxicity, handling, safety and cost”). Schaap reflects that understanding; in embodiments, Schaap describes the removal (e.g., evaporation) of organic solvents from crude oil to obtain a refined oil. MARA-1005, [0112], [0121], [0130]. Schaap further discloses a refined oil obtained by extraction using a solvent that

results in an oil with no more than 1 ppm (or undetectable levels) of that solvent in the final composition. MARA-1005, [0085] (Table). Thus, Schaap's refined oil would contain less than 5 wt.% of an organic solvent in total extracted microbial lipid composition. *Id.*

Similarly, application of Kralovec's refinement methods would eliminate and/or reduce the quantity of solvents present. Kralovec teaches using solvents that are "compatible with human consumption," for example, it teaches that "water is a preferred solvent." MARA-1030, 34:17-19; MARA-1003 ¶¶107-108. Furthermore, Kralovec teaches that its methods steps can "be performed...in the absence of solvent." MARA-1030, 23:15-17. Accordingly, a PHOSITA would have understood that refining Schaap's oils according to Kralovec's methods would not introduce residual solvent, meeting [3d] and rendering it obvious. MARA-1003, ¶¶107-110.

B. GROUND 2: Claims 1-7 are obvious over Schaap in view of Komazawa

1. Schaap

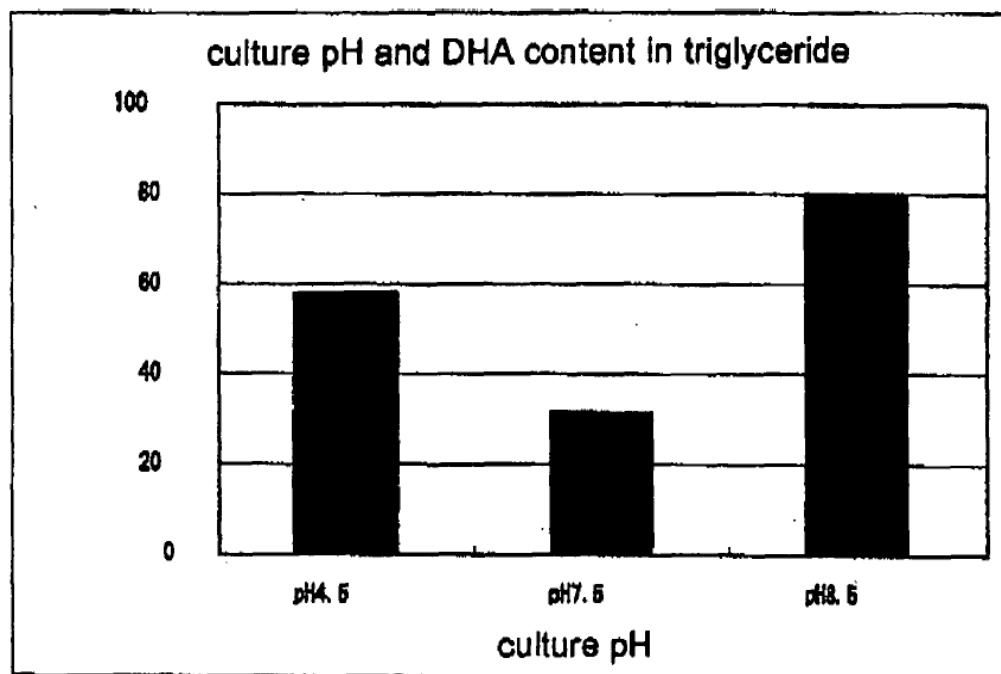
See §III.A.1, *supra*; MARA-1003, ¶111.

2. Komazawa

Komazawa "relates to a novel microorganism having an ability of producing docosahexaenoic acid (DHA) and the use of said microorganism." MARA-1015, [0001]. 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, ¶112.

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]; MARA-1003, ¶113; *see also* FIG. 3.



MARA-1015, FIG. 3.

3. Schaap-Komazawa Combination

1) DHA as the preferred PUFA

As discussed (§III.A.3.1, *supra*), it would have been obvious for a PHOSITA to have sought microbial oils having high levels of DHA as the preferred PUFA based on Schaap's teachings and other prior art available before the Critical Date. MARA-1005, [0056]; MARA-1030, 1:9-11; MARA-1003, ¶¶114-115. A PHOSITA would have been motivated to obtain DHA as the preferred PUFA in Schaap's extracted microbial oil for the reasons discussed above.

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

Komazawa provides methods for "culturing the Thraustochytrium strain having an ability of producing docosahexaenoic acid in a medium, and collecting docosahexaenoic acid-containing fat and oil from the culture product." MARA-1015, cl.3. It would have been obvious for a PHOSITA to combine the teachings of Schaap, directed to microbial oils having high levels of a preferred PUFA (DHA) as triglycerides, with Komazawa since it "provid[es] a microorganism which has a high ability of producing docosahexaenoic acid." MARA-1005, [0056], MARA-1015, Abstract; MARA-1003, ¶115. Specifically, a PHOSITA would have found it obvious to implement Komazawa's methods to Schaap's extracted microbial oil to increase the amount of DHA for at least the recognized health benefits associated with DHA, as discussed earlier (*see* §III.A.3.1; MARA-

1003, ¶70, *supra*), as well as the additional following reasons.

First, a PHOSITA would have been motivated to apply Komazawa's culturing methods to Schaap's teaching to obtain an extracted microbial oil with an increased DHA content because "purifying and concentrating PUFA's [sic] in a triglyceride form is generally desired." MARA-1030, 2:7-8; MARA-1003, ¶116. It would have been well-known that fewer unwanted components in a microbial oil resulting from an increased amount of DHA content would be desirable because if the "oil contains a variety of polyunsaturated fatty acids such as arachidonic acid or icosapentaenoic acid (EPA), it is likely to be oxidized" it would be "difficult to obtain fat and oil having stable quality." MARA-1015, [0003]; MARA-1003, ¶116. Furthermore, Komazawa also teaches that "in the field of medicines...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, ¶¶117-118.

Second, a PHOSITA would have been motivated to apply Komazawa's organism culturing techniques to Schaap's teachings for obtaining an extracted microbial oil because "[DHA] is a useful substance, the use of which has drawn attention in the fields of medicines and food products"; as such, it would be

generally desirable to have sources containing increased amounts of DHA.

MARA-1015, [0002], MARA-1003, ¶¶117-118.

Third, a PHOSITA would have been motivated to apply Komazawa's methods to Schaap's teachings because such combinations reflect nothing more than the use of a known technology (e.g., provide a desired microorganism) to improve similar oils (e.g., extracted microbial oils) according to known methods (e.g. culturing and oil extraction methods) to yield predictable results (e.g., obtain oil with an increased concentration of a desired PUFA, e.g., DHA). *KSR*, 550 U.S. at 417; MARA-1003, ¶119.

A PHOSITA would have expected to be successful in applying Komazawa's culturing techniques to increase the concentration of the preferred PUFA (i.e., DHA) in the microbial oil. MARA-1005, [0065]; MARA-1003, ¶119. Moreover, a PHOSITA would have naturally considered Komazawa's methods for providing a high DHA-producing microorganism because Schaap discloses that "microbial oil may comprise at least 10, 35, 40 or 45% or more of a desired PUFA." MARA-1005, [0056]; MARA-1003, ¶¶119-120. Thus, a PHOSITA would have looked to increase the levels of the preferred PUFA in Schaap's oils by looking to references such as Komazawa. MARA-1003, ¶¶119-120.

Moreover, a PHOSITA would have expected success in using Komazawa's culturing techniques for obtaining increased amounts of the preferred PUFA (i.e.,

DHA) particularly in the context of an extracted microbial oil given that Schaap and Komazawa teach that their oils are microbial/algal in origin and so have similar characteristics. MARA-1005, [0046]; MARA-1015, [0001]; MARA-1003, ¶¶119-120. Both acknowledge their oils are specific to omega-3 PUFAs, and even more specifically DHA. MARA-1005, [0045]-[0046], [0053]; MARA-1015, [0001]. Furthermore, both Schaap and Komazawa acknowledge similar uses for their oils, such as human nutritional uses. Schaap, for example, teaches that its resultant oil is “particularly suitable for nutritional purposes, and can be added to (human) foods.” MARA-1005, [0066]. Komazawa too discloses that its oils are used in “the field of functional foods.” MARA-1015, [0002].

4. Analysis

Claim 1

[1pre]

See §III.A.4 [3pre], *supra*. MARA-1003, ¶121.

[1a]

See §III.A.4[3a], *supra*. MARA-1003, ¶122.

[1b]

Schaap-Komazawa discloses and/or renders obvious [1b]. MARA-1003, ¶123; *see also* §III.A.4[3b], *supra*.

Schaap teaches that “microbial oil may comprise at least...45% or more of a desired PUFA[.]” MARA-1005, [0044]-[0053], [0056], cl. 5; MARA-1003, ¶124.

Indeed, Schaap recognizes DHA as a “preferred” PUFA. MARA-1005, [0045]-[0046], [0053], cl. 10. As explained above (§III.A.3.1, *supra*), DHA was well-known and sought-after for its many benefits and therefore would have been sought-after as a preferred PUFA. MARA-1003, ¶124; *see also* MARA-1010, 117.

Moreover, a PHOSITA would have understood that *Thraustochytrium* microbes, such as those disclosed in Schaap, would have produced oil that was “preferably 50% by weight or more” DHA. MARA-1015, [0058], [0108]; MARA-1009, 29; MARA-1032, 27-31 (Table 2.5 discloses 67.2, 65.6, 67.8, 63.7, 64.3, 62.4 and other percentages of DHA). Accordingly, a PHOSITA would have understood from Schaap’s disclosure that its composition comprises at least 50 wt.% DHA, or even 60 wt.%, since there *is* “45% or more” of DHA, a “[p]referred” PUFA. MARA-1005, [0053]. *See Peterson*, 315 F.3d at 1329-30 (“[E]ven a slight overlap in range establishes a *prima facie* case of obviousness.”).

Additionally, a PHOSITA would have understood that in the Schaap microbial oil, most of the PUFAs would be in triglyceride form. MARA-1003, ¶¶125-126. Schaap’s disclosures confirm this: “Preferably, the microbial oil has a triglyceride content of from 90 to 100%” which is “optimally at least 95% or 98% of the oil.” MARA-1005, [0055]-[0056]; *see also* [0085] (Table), [0089]. A PHOSITA would have understood since the majority of Schaap’s microbial oil is made up of triglycerides (e.g., up to 100%), the majority of Schaap’s PUFAs were

also likely present in the triglyceride form. MARA-1003, ¶¶125-129.

As discussed above (§III.B.3, *supra*), in the combination, a PHOSITA would have been motivated to apply Komazawa's culturing methods to Schaap's extracted microbial oil to increase its DHA content. MARA-1003, ¶128. In doing so, 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.

[1c]

Schaap-Komazawa discloses and/or renders obvious [1c]. MARA-1003, ¶¶130-133.

It was well-known prior to the Critical Date that microorganisms typically produce oil compositions containing multiple PUFAs. MARA-1003, ¶131. In particular, *thraustochytrids* were known to produce both DHA and DPA n-6. MARA-1009, 27; MARA-1018, [0571]; MARA-1020, 385. Schaap discloses that its oils are microbially derived from sources, including those from *Thraustochytrium*, and it was well known before the Critical Date that preferred microbial strains containing a high level of DHA (e.g., 61%) and a low level of DPA n-6 (e.g., 3.4%) were available. MARA-1005, [0045]; MARA-1009, 27; MARA-1003, ¶131.

Furthermore, in the combination (*see* §III.B.3, *supra*), a PHOSITA would

have been motivated to apply Komazawa's methods to Schaap's extracted microbial oil to increase its DHA content. MARA-1003, ¶132. In doing so, Komazawa's method can be used to produce an exemplary oil having a DPA n-6 component of 3.2%. MARA-1015, [0108]. It would have therefore been obvious and/or understood that the extracted microbial oil of the combination produces a concentration of oils that falls within the range of 0.5% by weight to 6% by weight DPA n-6 of the triglyceride fraction. *See* MARA-1009, 27, Table 2.

[1d]

See §III.A.4[3c], *supra*. MARA-1003, ¶¶134-136.

[1e]

See §III.A.4[3d], *supra*. MARA-1003, ¶¶137-142.

Claim 2

Schaap-Komazawa renders obvious the following limitations of claim 2 as explained above (§III.B.4, *supra*) for the corresponding claim 1 limitations listed in the table below. MARA-1003, ¶¶143-151.

Claim 2 Limitation	Corresponding Limitations
[2pre]	[1pre]
[2a]	[1a]
[2b]	[1b]
[2c]	[1c]
[2e]	[1d]
[2f]	[1e]

[2d]

Schaap-Komazawa discloses and/or renders obvious [2d]. MARA-1003, ¶¶147-149. Any disclosure that satisfies [1b]-[1c] and [2b]-[2c] will also satisfy [2d]. MARA-1003, ¶¶147-149. That is because if an extracted microbial lipid of the combination contains the DHA (40%) and the maximum amount of DPA n-6 (6%), they will be present in a ratio greater than 6:1. *Id.*

Claim 3

Schaap-Komazawa renders obvious the following limitations of claim 3 as explained above (§III.B.4, *supra*) for the corresponding claim 1 limitations listed in the table below. MARA-1003, ¶¶152-156.

Claim 3 Limitation	Corresponding Limitations
[3pre]	[1pre]
[3a]	[1a]
[3b]	[1b]
[3c]	[1d]
[3d]	[1e]

Claim 4

[4]

Schaap-Komazawa discloses and/or renders obvious [4]. MARA-1003, ¶¶157-158. A PHOSITA would have found it obvious that the combination oil has peroxide values of 5 or less since Schaap discloses that its oils' peroxide value “ranged from 1.3 (or 0.8) to 0.4.” MARA-1005, [0081], [0122]-[0123]; MARA-

1003, ¶¶157-158.

Claim 5

[5]

Schaap-Komazawa discloses and/or renders obvious [5]. MARA-1003, ¶¶159-162. Schaap discloses microbial oils having a phospholipid concentration less than 0.05 wt.% of the total composition. MARA-1005, [0085]. Schaap's crude oils have "a phosphorus content of at least 2, 3, or 5 mg/kg." MARA-1005, [0091]. A PHOSITA would have understood that "mg/kg" is equivalent to an oil with a phosphorus content of 2, 3, or 5 ppm. MARA-1003, ¶¶161-162.

Claim 6

[6]

Schaap-Komazawa discloses and/or renders obvious [6]. MARA-1003, ¶163. Schaap's "microbial oil may be a crude oil." MARA-1005, [0057].

Claim 7

[7]

Schaap-Komazawa discloses and/or renders obvious [7]. MARA-1003, ¶164. Schaap's "crude PUFA containing oil" "can be subjected to one or more refining steps." MARA-1005, [0065].

**C. GROUND 3: Claims 1-7 are obvious over Bijl in view of
Nichols-I and Schaap**

1. Bijl

Bijl, like the '578 patent, is directed to microbial oils. MARA-1001, 1:16-

23, 2:16-22; MARA-1008, 2:30-36, 9:5-7. Bijl also discloses high quality microbial oils sourced from naturally-occurring microorganisms and processes for obtaining quality microbial oils. MARA-1001, 14:16-16:3; MARA-1008, 12:22-37; 2:35-3:2; MARA-1003, ¶¶165.

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, low monoglyceride content, a light color, a low level of off-flavors, and/or a low *p-anisidine* value. *Id.*, 5:14-19. Bijl's microbial oils are usable in food, nutritional supplements, and cosmetics. *Id.*, 4:13-18; MARA-1003, ¶166.

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, ¶167.

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, ¶168.

Use of 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, 9:5-19, 9:20-25; MARA-1003, ¶169.

2. 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. *Id.*, 27 (Table 1), 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 (Table 2); MARA-1003, ¶170. Strain O is "particularly attractive" because it "contains very high levels of DHA (61%)." MARA-1009, 27.

Nichols-I also discloses uses and benefits of microbially-derived oils. *Id.*,

26, 28. 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. *Id.*, 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, ¶171.

3. Schaap

See § III.A.1 (*supra*).

4. Bijl-Nichols-I-Schaap Combination

1) Preferred Microbial Strains

A PHOSITA would have found it obvious to implement Nichols-I's teachings of using a preferred strain of microorganisms (e.g., strain O) as a microbial source for Bijl's extracted microbial oil for at least the following reasons. MARA-1003, ¶¶174-182.

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, ¶175.

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, ¶176.

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, ¶¶172, 177.

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, ¶178. As Nichols-I notes, DHA is "beneficial against various human disorders." MARA-1009, 26; MARA-1003, ¶171. 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, 117.

Fifth, a PHOSITA would have been motivated to use Nichols-I's preferred microbial strains as a source for Bijl's extracted oil because "DPA(6) is only a minor component in our strain O under the culture conditions employed, making this strain [O] particularly interesting." MARA-1009, 27; MARA-1003, ¶179.

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, ¶¶180-182; MARA-1010, 78-80, 88-89, 179-200. 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 reasonably expected success in combining Bijl with Nichols-I. Bijl and Nichols-I both relate to the creation of microbial lipids using culturing techniques. MARA-1008, 7:2-11; MARA-1009, 27-28. Both references teach the same sources of those microbial lipids: algae, fungi, dinoflagellates, and other diatoms. MARA-1008, 12:22-37; MARA-1009, 27; *see also* MARA-1018, [0569]-[0570] (Table 3); MARA-1020, 384-385. And both teach that the desired product is one of high enough quality for use in the human diet. MARA-1008, 14:23-27; MARA-1009, 27-28. Furthermore, Bijl discloses that its processes are compatible with a wide range of natural sources, e.g., *Cryptocodinium* and *Thraustochytrium*, which are also disclosed in Nichols-I. MARA-1008, 6:3-11; 13:19-31; MARA-1009, 27; MARA-1003, ¶183.

2) Improved Processes for Obtaining Microbial Oil

A PHOSITA would have also found it obvious to combine the teachings of Bijl-Nichols-I and Schaap to yield a better oil quality by using improved techniques of pasteurizing and extracting cells, as taught by Schaap, in Bijl's method. MARA-1003, ¶184; MARA-1005, Abstract, [0001].

Specifically, Schaap describes already known processes that involve heating microbial cells. MARA-1005, [0007]. Schaap cites to Bijl (MARA-1008), stating that it discloses that microbial cells were pasteurized prior to extraction. MARA-1005, [0007]. Schaap teaches that its new processing techniques can "improve the quality of the oil that can be extracted from the pasteurised cells," as compared to the already known methods, such as those disclosed by Bijl. *Id.* In fact, Schaap further refers to Bijl in its disclosure as providing already known techniques for extraction as well as other oil processing related methods. *Id.*, [0064]. Hence, a PHOSITA would have naturally sought to apply the improvements of Schaap to Bijl's teachings to advance Bijl's goal of obtaining a high quality polyunsaturated fatty acid-(PUFA) containing oil with a high triglyceride content. MARA-1008, 4:2-5; MARA-1003, ¶¶184-185.

A PHOSITA would have been motivated to apply Schaap's improved processing techniques for pasteurizing and extracting to Bijl-Nichols-I for at least the following reasons.

First, a PHOSITA would have been motivated to apply Schaap's pasteurizing and extracting processes to obtain the oil of Bijl-Nichols-I because doing so would "improve the quality of the oil," which "may oxidise less, or be less oxidized[.]" MARA-1005, [0007]; MARA-1003, ¶187.

Second, a PHOSITA would have been motivated to implement Schaap's pasteurizing and extracting processes because doing so would yield a "resulting oil" "having a peroxide value (POV) of less than 1.5 and an anisidine value (AnV) of less than 1.0," which are attributes associated with a "better quality" oil. MARA-1005, Abstract, [0007]; MARA-1003, ¶¶187-188.

Third, a PHOSITA would have been motivated to apply Schaap's pasteurizing and extracting processes to Bijl's method to yield the Bijl-Nichols-I oil because the "new pasteurisation process is more efficient because it requires less energy." MARA-1005, [0007]; MARA-1003, ¶189.

Fourth, a PHOSITA would have been motivated to implement Schaap's improved processing techniques for pasteurizing and extracting to Bijl-Nichols-I's method for obtaining an oil because doing so would have amounted to nothing more than the use of a known technique to improve similar oils in the same way and combining prior art elements according to known methods to yield predictable results. *KSR*, 550 U.S. at 417; MARA-1003, ¶190.

For at least the reasons provided above, a PHOSITA would have found it

obvious to combine the teachings of Bijl and Nichols-I with the disclosures of Schaap to obtain an improved PUFA-containing oil with a high triglyceride content and also to obtain an oil at reduced costs with less energy expenditure. MARA-1005, [0007]; MARA-1003, ¶191.

A PHOSITA would also have reasonably expected success in combining Bijl-Nichols-I with Schaap. MARA-1003, ¶192. Bijl, Nichols-I, and Schaap all relate to the extraction of microbial lipids. MARA-1005, [0013], [0062]-[0066]; MARA-1008, 2:30-32; MARA-1009, 27-28. All three references teach the same and/or similar sources of those microbial lipids: algae, bacteria, fungi, etc. MARA-1005, [0054], [0060]; MARA-1008, 12:22-37; MARA-1009, 27; *see also* MARA-1018, [0569]-[0570]. And each reference teaches that the desired product is one of high enough quality for use in the human diet. MARA-1005, [0095], [0096]-[0097]; MARA-1008, 14:23-27; MARA-1009, 27-28. Furthermore, Schaap discloses that its processes are compatible with natural sources, including *Thraustochytrium*, which are also disclosed in Bijl and Nichols-I. MARA-1005, [0046], [0054], [0071], cls. 12-13; MARA-1008, 6:3-11; 13:19-31; MARA-1009, 27; MARA-1003, ¶183.

5. Analysis

Claim 1

[1pre]

Bijl-Nichols-I-Schaap discloses and/or renders obvious [1pre]. MARA-

1003, ¶¶193-196.

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, like the ’578 patent, Bijl uses lipids and oils interchangeably, noting that “PUFA (oil) which has been extracted can be used” with or without further refining. *Id.*, 9:20-22.

Extracted microbial lipids were well known to a PHOSITA prior to the Critical Date. For example, other prior art references, such as Singh, describe an extracted microbial lipid. *See* MARA-1018. Singh discloses that LC-PUFA “may be present as a mixture of forms in the lipid of a cell or a purified oil or lipid extracted from cells, tissues, or organisms.” *Id.*, [0294].

[1a]

Bijl-Nichols-I-Schaap discloses and/or renders obvious [1a]. MARA-1003, ¶¶197-202.

As discussed previously (§III.A.4, [3a], *supra*), the ’578 patent does not define the term “lipid fraction.” However, a PHOSITA would have understood that the term “lipid fraction” refers to either: (1) only the lipid portion of the extracted microbial lipid, exclusive of solvent; or (2) the entire composition

associated with extracted microbial lipid, including residual solvent.

To the extent that “lipid fraction” means the entire extracted microbial oil, the triglyceride fraction comprises at least 70 wt.% of the total lipid composition. MARA-1003, ¶198-199. The proposed combination discloses and/or renders obvious the lipid fraction under either interpretation. *Id.*, ¶199.

For example, 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.

Indeed, triglyceride-rich oils were well known to a PHOSITA prior to the Critical Date. Consistent with the teachings in Bijl, other references (e.g., Schaap and Singh) also disclosed triglyceride-rich oils. MARA-1005, [0055] (“optimally at least 95% or 98% of the oil”); MARA-1018, [0294] (“oil comprising at least 75% or 85% triacylglycerols...said triacylglycerols comprising the LC-PUFA”).

[1b]

Bijl-Nichols-I-Schaap discloses and/or renders obvious [1b]. MARA-1003, ¶¶203-207.

As discussed above (§III.B.4, *supra*), in the proposed combination, 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 a desired PUFA (e.g., DHA).

MARA-1003, ¶204. The PHOSITA would have done so because “[s]train O is particularly attractive as it contains very high levels of DHA (61%),” with DPA n-6 being “only a minor component.” MARA-1009, 27 (identifying 3.4% DPA n-6); MARA-1003, ¶204. Also, it would have been obvious to a PHOSITA to combine the teachings of Bijl and Nichols-I as doing so would have amounted to nothing more than the use of a known technique to improve similar oils in the same way and combining prior art elements according to known methods to yield predictable results. MARA-1003, ¶204.

A PHOSITA would have found it obvious that the DHA content of the triglyceride fraction is at least 50 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, Table 2; MARA-1003, ¶205. Specifically, Nichols-I discloses that *Thraustochytrium* strain O contains “very high levels of DHA (61%).” MARA-1009, 27; MARA-1018, [0571]; MARA-1020, 384-385, Table 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 50 wt.%, and even greater than 60 wt.%. MARA-1032, 27-31 (Table 2.5 discloses 67.2, 65.6, 67.8, 63.7, 64.3, 62.4 and other percentages DHA); MARA-1015, [0108], [0113]-[0114], [0016], Fig. 3. For example, Komazawa is one example that discloses a

Thraustochytrium strain (LFF1 strain) that contains DHA components ranging from 62% to 84%. 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, ¶206. In fact, Bijl discloses that DHA is a preferred PUFA associated with the triglycerides present in its oil: the invention "preferably comprises a triglyceride, such as one of the PUFAs previously mentioned," such as DHA. MARA-1008, 6:3-5; 7:18-19. Furthermore, a PHOSITA would have known that microbial oils having a DHA content of approx. 60 wt.% in the triglyceride fraction would have been consistent with teachings of other prior art: Komazawa discloses exemplary *Thraustochytrium* strains (e.g., LFF1 strain) including DHA components in the triglyceride (TAG) fraction that range from "around 40%" to "80% or more," depending on the culturing conditions, and Apt discloses DHA in the TAG fraction in amounts of 58.1 wt.% and 60.4 wt.%. MARA-1015, [0016], Fig. 3; MARA-1017, Table 6 (C22:6 N3*...58.1%), Table 8 (C22:6 N3*...60.4%).

Moreover, the PHOSITA would have understood that in Bijl's microbial oil, most of the PUFAs (DHA) would be in triglyceride form because Bijl discloses a preference for high levels of triglycerides, e.g., "a triglyceride content $\geq$ 97%." MARA-1008, 4:24-30; MARA-1003, ¶¶206-207.

The combination of Bijl and Nichols-I would have led a PHOSITA to obtain an oil derived from Strain O thraustochytrids, which would contain high levels of triglycerides and 61 wt.% DHA. MARA-1003, ¶¶203-204. That in turn discloses or renders obvious [1a] and [1b]. *Id.*

[1c]

Bijl-Nichols-I-Schaap discloses and/or renders obvious [1c]. MARA-1003, ¶¶208-214.

Since [1a] requires a triglyceride fraction of at least about 70 wt.% of the lipid fraction, the DPA n-6 content of between 0.5 and 6 wt.% of such a triglyceride fraction (i.e., 70 wt.% of the lipid fraction) can be expressed as the DPA n-6 content constituting between 0.35 and 4.2 wt.% of the lipid fraction when the triglyceride fraction is 70 wt.%. MARA-1003, ¶209.

Bijl discloses microbial oil compositions that “predominantly contain one particular polyunsaturated fatty acid” but “can additionally contain other polyunsaturated fatty acids in lesser amounts.” MARA-1008, 6:11-14; *see also id.*, 5:24-29, 6:23-26. The PUFA in Bijl expressly includes omega-3 or omega-6 “C18, C20, or C22” polyunsaturated fatty acids. *Id.*, 4:5-8. DPA n-6 is a C22 omega-6 fatty acid. MARA-1003, ¶210. Bijl therefore discloses compositions that can comprise both DHA and DPA n-6. *Id.*

It was well-known prior to the Critical Date that microorganisms typically

produce oil compositions containing multiple PUFAs. *Id.*, ¶211. Depending on the species selected, differing oil compositions result: “In general, green algae either do not contain or have only very low levels of EPA and DHA; diatoms contain elevated EPA, as do eustigmatophytes; dinoflagellates contain DHA and other C18 PUFA; and red algae can contain elevated proportions of 20:4 ω -6, arachidonic acid (AA).” MARA-1009, 27; MARA-1020, 384. In particular, thraustochytrids were known to produce both DHA and DPA n-6. MARA-1009, 27; MARA-1018, [0571]; MARA-1020, 385. A PHOSITA would have understood, then, that culturing thraustochytrids would result in a microbial oil composition containing both DHA as well as DPA n-6. MARA-1003, ¶211.

As discussed above (III.B.4, *supra*), a PHOSITA would have used Nichols-I’s preferred strains (e.g., O thraustochytrids) in producing Bijl’s extracted microbial oil. A PHOSITA would have understood that, in the proposed combination, the extracted microbial oil includes DPA n-6 content of the triglyceride fraction within the range of 0.5% by weight to 6% by weight. Specifically, Nichols-I explains that the DPA n-6 concentration of oils extracted from strain O thraustochytrids (i.e. 3.4 wt.% DPA n-6) falls within the range of 0.5% by weight to 6% by weight of the triglyceride fraction. MARA-1009, 27, Table 2. Indeed, it was well known to a PHOSITA based on the prior art available before the Critical Date that “[s]train O” was a specific strain of Australian

thraustochytrid that yielded both DHA and DPA n-6 at 3.4 wt.% of the total lipid composition. *Id.*; MARA-1018, [0571]; MARA-1020, 384-385, Table 2; *see also* MARA-1032, 27-31 (Table 2.5 discloses 67.2, 65.6, 67.8, 63.7, 64.3, 62.4 and other percentages DHA and low percentages of DPA n-6).

Furthermore, a PHOSITA would have been informed by other prior art, such as Komazawa, which teaches that certain *Thraustochytrium* strains (e.g., LFF1 strain) include DPA n-6 components in an amount of 3.2%. MARA-1015, [0016], Fig. 3. Also, it was well known that there were strains of thraustochytrid (ATCC Accession No. PTA-9695) that contained between 0.4 to 2.8 wt.% DPA n-6. MARA-1015, Table 5 (C22:5 N3*...2.7).

A PHOSITA would have understood that most of Bijl's PUFAs (DHA) would be in triglyceride form because Bijl discloses a preference for high levels of triglycerides, e.g., "a triglyceride content $\geq$ 97%." MARA-1008, 4:24-30, 6:3-5, 7:18-19; MARA-1003, ¶¶206-207. And because a PHOSITA would have understood that "the oil of the present invention can be microbially derived," (MARA-1008, 3:3-5), they also would have understood that using Nichols-I's strain O thraustochytrid as a microbial source to produce Bijl's extracted microbial oil renders obvious [1c]. MARA-1003, ¶¶211-214.

[1d]

Bijl-Nichols-I-Schaap discloses and/or renders obvious [1d]. MARA-1003,

¶¶215-217.

Bijl generally discloses high-quality oils having low anisidine values that are less than 26. MARA-1008, 5:20-21; MARA-1003, ¶216. A PHOSITA would have understood that anisidine values reflect the quality of an oil because “anisidine is a test for aldehydes, a product of degradation by oxidation.” MARA-1008, 5:18-19; MARA-1003, ¶216. For example, the extracted microbial oils of Bijl have a “low anisidine value” that “typically varies from 0.1 to 5” and “preferably from 0.1 to 2, more preferably from 0.1 to 1.” MARA-1008, 5:20-21. Indeed, Bijl discloses a prepared Batch A in which the anisidine value was “<1.0,” which discloses an anisidine value overlapping the recited range of 0.5 to 26. *Id.*, 49:11-18; MARA-1003, ¶216. Bijl further discloses refining three batches of oils, resulting in oils with anisidine values of 4.1, 1.9, and 3.1, respectively. MARA-1008, 50:4-16.

[1e]

Bijl-Nichols-I-Schaap discloses and/or renders obvious [1e] for at least the following reasons. MARA-1003, ¶¶218-227.

1) Element [1e] is Optional

As discussed previously (§III.A.2, *supra*), [1e] is an optional element for

which prior art disclosure is not necessary to meet the claim element.⁷ See

§III.A.2; *AC Techs*, 912 F.3d at 1367. Accordingly, Bijl-Nichols-I discloses and/or renders obvious all of the elements of claim 1. MARA-1003, ¶¶14, 193-227.

2) Element [1e] is Rendered Obvious by Bijl

Even if the presence of some organic solvent in an amount less than 5 wt.% of the lipid was required, the proposed combination renders this element obvious based on Bijl's disclosure. MARA-1003, ¶¶220-227. Bijl's process for obtaining an oil utilizes a solvent to perform extraction, passing it over granules of biomass. MARA-1008, 27:21-34. Bijl explains that "the PUFA is extracted from the dried granules using a solvent," which can be "[a]ny suitable solvent known to a person skilled in the art[.]" *Id.*, 8:36-9:4. A column is filled with dried granules and then solvent is recirculated multiple times, extracting the PUFA. *Id.*, 27:21-34; MARA-1003, ¶220.

Bijl uses significantly reduced amounts of solvent in its process. MARA-1008, 27:11-13. Bijl explains that "20 to 30 times less solvent" is needed to perform the extraction process. *Id.* Since less solvent is used, "significant economic saving" and minimization of "emission problems" can be attained. *Id.*, 27:13-15. In this way, Bijl's "invention can enable a cost effective and efficient

⁷ Elements [2f] and [3d] are also optional for the same reasons as provided for [1e].

extraction of the PUFA oil, and provide an oil of a particularly high quality” in part because “the dried granules may require reduced amounts of solvent for the extraction process” and “the release of the used solvent from the biomass,” or “desolventising toasting,” “can be achieved more efficiently[.]” *Id.*, 9:5-16. Indeed, Bijl notes that any residual organic solvent present in the crude oil is removable via evaporation. *Id.*, 31:12-13; MARA-1003, ¶221.

Furthermore, Bijl explains that “[t]he PUFA (oil) which has been extracted can be used in that state without further processing” and, specifically, notes that “[t]he residue resulting after (solvent) extraction (and even after desolventising toasting) can be used as a feed stuff or a feed component (such as for animals).” MARA-1008, 31:12-13. Based on this disclosure provided by Bijl and other related references, a PHOSITA would have understood that a lipid composition suitable for animal consumption, as described by Bijl, would contain less than 5% by weight of an organic solvent to facilitate safe consumption. *See, e.g.*, MARA-1005, [0066], [0094]-[0101], [0085]; MARA-1003, ¶¶222-223.

Moreover, to the extent that Bijl is not found to disclose a weight percent of organic solvent present in the extracted lipid composition, a PHOSITA would have understood that the amount of the organic solvent would be less than 5 wt.% because Bijl’s disclosure is cited by the later-filed Schaap application for its disclosure of describing suitable techniques of extracting a microbial PUFA

containing oil. *See* MARA-1005, [0064]. Hence, a PHOSITA would have understood that Bijl's extraction techniques were applied and/or at least applicable to Schaap's process for obtaining its resulting oils. MARA-1003, ¶223. Furthermore, Schaap discloses that each of its extracted oils contain solvent (e.g., hexane) in an amount of 100-2,000 ppm (or 0.01 wt.% to 0.02 wt.% organic solvent) as a crude oil, and in undetectable or an amount of less than 1 ppm as a refined oil. MARA-1005, [0085]-[0088]. It would have been obvious to a PHOSITA that Bijl's techniques for extraction, which are the same techniques cited in Schaap, would have resulted in oils having the same or similar organic solvent residual amounts as those of Schaap. MARA-1003, ¶¶224-227. Accordingly, a PHOSITA would have found obvious from these disclosures that Bijl's microbial lipid contains less than 5 wt.% organic solvent. *Id.*

3) Element [1e] is Rendered Obvious by the Combination

The "less than 5% by weight of an organic solvent" limitation is further rendered obvious by the proposed combination of Bijl, Nichol-I and Schaap because a PHOSITA implementing Bijl would have applied the process techniques taught by Schaap to obtain an improved oil. MARA-1003, ¶¶224-227. Similar to Bijl, Schaap teaches extracting an oil from a biomass or broth that has been subjected to a pasteurization process. MARA-1005, Abstract. Schaap's processes, however, "result in a smaller energy input (and so a reduction in costs)" as well as

“a better quality (and less oxidised) oil[.]” *Id.*

A PHOSITA would have applied the teachings of Schaap for preparing (e.g., pasteurizing) and extracting microbial oils to Bijl’s process for obtaining an oil for at least the following reasons: (1) to “improve the quality of the oil,” which “may oxidise less, or be less oxidized”; (2) to produce a “resulting oil” with “a low peroxide value (POV)”; (3) to obtain an improved quality oil having a low anisidine value (AnV); and (4) because its process “is more efficient” and “requires less energy.” MARA-1005, [0007]; MARA-1003, ¶¶225-227.

And by applying Schaap’s processing techniques in Bijl’s method for pasteurizing and extracting oil, it would have been obvious to a PHOSITA that the proposed combination would yield an oil having the improved characteristics disclosed by Schaap. Schaap discloses that its process “improve[s] the quality of the oil that can be extracted from the pasteurised cells.” MARA-1005, [0007]. Schaap further describes that “the crude oil in the present invention” includes features such as “a solvent (e.g. hexane) content of from 10, 50 or 100 ppm up to 1000, 1500 or 2000 ppm,” which are all values that fall within the less than 5 wt.% limit of [1e]. MARA-1005, [0086]-[0088]; MARA-1003, ¶¶226-227. A PHOSITA would have understood these disclosures to mean that less than 5 wt.% organic solvent is present in the resulting microbial lipid. MARA-1003, ¶¶226-227.

For the reasons provided above, the combination of Bijl, Nichols-I, and Schaap discloses and/or renders obvious [1e]. MARA-1003, ¶227.

Claim 2

Bijl-Nichols-I-Schaap renders obvious the following limitations of claim 2 as explained above (§III.C.5, *supra*) for the corresponding claim 1 limitations listed in the table below. MARA-1003, ¶¶228-238.

Claim 2 Limitation	Corresponding Limitations
[2pre]	[1pre]
[2a]	[1a]
[2b]	[1b]
[2c]	[1c]
[2e]	[1d]
[2f]	[1e]

[2d]

Bijl-Nichols-I-Schaap discloses and/or renders obvious [2d]. *See* [2b]-[2c], *supra*; MARA-1003, ¶¶232-236. Any disclosure that satisfies [1b]-[1c] and [2b]-[2c] will also satisfy [2d]. MARA-1003, ¶¶233-236.

Claim 3

Bijl-Nichols-I-Schaap renders obvious the following limitations of claim 3 as explained above (§III.C.5, *supra*) for the corresponding claim 1 limitations listed in the table below. MARA-1003, ¶¶239-243.

Claim 3 Limitation	Corresponding Limitations
[3pre]	[1pre]
[3a]	[1a]
[3b]	[1b]
[3c]	[1d]
[3d]	[1e]

Claim 4

[4]

Bijl-Nichols-I-Schaap discloses and/or renders obvious [4]. MARA-1003, ¶¶244-247. Bijl discloses crude oil with peroxide values of 2.7, 1.3, and 1.3. MARA-1008, 49:11-16. Additionally, Bijl further discloses refined batches with peroxide values of 1.6, 0.8, and 0.4. *Id.*, 50:4-16.

Claim 5

[5]

Bijl-Nichols-I-Schaap discloses and/or renders obvious [5]. MARA-1003, ¶¶248-254. Bijl discloses microbial oils with phospholipid concentrations less than 0.05 wt.% of the total composition. MARA-1008, 50:4-16. A PHOSITA would have understood that, on a ppm basis, the entire phospholipid concentration would have encompassed less than 100 ppm of phosphorus. MARA-1003, ¶¶250-254.

Claim 6

[6]

Bijl-Nichols-I-Schaap discloses and/or renders obvious [6]. MARA-1003, ¶¶255-256. For example, Bijl describes preparing “[b]atches of crude oil” where “[t]he thus-extracted lipid is in a crude form[.]” MARA-1008, 49:3-5, 1:32-2:3; *see also id.*, 31:13-14; MARA-1003, ¶255.

Claim 7

[7]

Bijl-Nichols-I-Schaap discloses and/or renders obvious [7]. MARA-1003, ¶¶257-258. For example, Bijl discloses, “[t]he thus-extracted lipid is in a crude form and so is often subjected to several refining steps.” MARA-1008, 2:1-2:3. Moreover, “for all oils destined for direct consumption,” refinement processes such as refining, bleaching, and deodorization are carried out. MARA-1010, 180-181.

D. GROUND 4: Claim 3 is obvious over Radianingtyas and Wang

1. Overview of Radianingtyas

Radianingtyas, like the ’578 patent, is directed to methods of culturing oil-producing microbes and extracting microbial oils rich in omega-3 fatty acids. MARA-1007, 1:27-2:2; MARA-1001 1:48-61, 2:8-12, 12:56-13:15.

Radianingtyas’s method includes extracting the biomass with solvents or via supercritical fluid extraction. MARA-1007, 32:10-14; MARA-1003, ¶¶259-260.

Radianingtyas’s resultant oils comprise unsaturated fatty acids with

approximately 96-100 wt.% triglycerides and constituent acids, including DHA and DPA n-6. MARA-1007, 33:1-2, 11:4-9. As Radianingtyas discloses 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, ¶261.

The parameters of Radianingtyas’s methods can be modified to obtain different yields of DHA, EPA, and/or DPA n-6. MARA-1007, 27:4-8. Modifying the “medium of an oil...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.” *Id.*, 27:15-28, 28:14-20, 30:15-17; MARA-1003, ¶262.

2. Overview of Wang

Wang, like the ’578 patent, is directed to creating higher quality oils derived from marine sources through processes that remove undesirable components. MARA-1006, [0005]-[0006], [0050]-[0074]; MARA-1001 1:48-61, 2:8-12; MARA-1003, ¶263. Wang also discloses a process that focuses on minimizing the cost to extract such improved oils while maintaining high yields of the same. MARA-1006, [0005]-[0007]; MARA-1001 1:48-61, 2:8-12.

The process of Wang utilizes adsorbents and temperature changes to modify the chemical composition and characteristics of derived crude oils. MARA-1006,

[0075], [0077]-[0078], [0147]-[0148], [0082]-[0084], [0086]-[0087]; MARA-1003, ¶264. This processing yields an oil with reduced levels of sterols. MARA-1006, [0021]-[0022]. Wang's oils contain a variety of fatty acids, including the omega-3 fatty acids DHA and DPA. *Id.*, [0050]-[0074]. In particular, Wang discloses that DHA is present in approximately 0-70 wt.% of the total composition weight. *Id.*, [0058]-[0059]. The total triglyceride content in Wang's oils is over 97 wt.% of the total composition. *Id.*, [0072]-[0074]; MARA-1003, ¶265.

Oils processed using Wang's method have *p-anisidine* values ranging from 1 to 25. *Id.*, [0069]-[0071], [0153], (Table 4); MARA-1003, ¶266.

3. Combination of Radianingtyas and Wang

A PHOSITA would have found obvious that combining the teachings of Radianingtyas for extracting microbial oils and the teachings of Wang for applying adsorbents and temperature-based applications on extracted oils would have resulted in an improved high quality oil. MARA-1003, ¶¶264-267; MARA-1007, 16:31-17:3; MARA-1006, [0024]; *see also id.*, [0170]-[0172] ("oil qualities" shown in Table 13). A PHOSITA would have naturally sought Wang's method of eliminating and/or reducing undesirable compounds and applied those methods to Radianingtyas's oil composition to yield a higher quality oil. MARA-1003, ¶268.

Specifically, a PHOSITA would be motivated to apply Wang's method of reducing undesirable compounds (e.g., cholesterol) to Radianingtyas's process for

extracting oil to improve the quality of the extracted oil for at least the following reasons.

First, doing so would improve the quality of the oil. MARA-1006, [0170]-[0172] (Table 13); MARA-1013, [0009]; MARA-1003, ¶269. A PHOSITA would have recognized that Wang’s process yields a more stable, higher-quality oil, e.g., an oil having a lower anisidine value. MARA-1003, ¶269.

Second, a PHOSITA would have been motivated to apply Wang’s method of reducing undesirable compounds (e.g., cholesterol) to Radianingtyas’s process for extracting oil to produce “stable” products that are able to meet “market realities and the ability to store and transport the product at readily attainable environmental conditions[.]” MARA-1007, 6:25-7:2; MARA-1003, ¶270.

Third, a PHOSITA would have been motivated to apply Wang’s process to Radianingtyas’s oil extraction process because a PHOSITA would have combined the teachings of Radianingtyas and Wang as doing so would have amounted to nothing more than the use of a known technique to improve similar oils in the same way and combining prior art elements according to known methods to yield predictable results. *KSR*, 550 U.S. at 417; MARA-1003, ¶271.

A PHOSITA would have a reasonable expectation of success in combining Radianingtyas’ and Wang’s teachings to produce an improved oil composition. MARA-1003, ¶272. Both Wang and Radianingtyas relate to the same field:

obtaining and processing microbial lipids from microorganisms to yield high quality microbial lipid compositions. MARA-1007, 1:22-26; MARA-1006, [0024]; MARA-1003, ¶272. Both Wang and Radianingtyas also teaches that differing yields of desired fatty acids are obtainable by culturing microbe-producing marine organisms in differing conditions. MARA-1007, 27:4-8; MARA-1006, [0144], [0159]; MARA-1003, ¶272.

4. Analysis

Claim 3

[3pre]

Radianingtyas-Wang discloses and/or renders obvious [3pre]. MARA-1003, ¶¶273-276. 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, 40:29-31, 1:27-31; *see also id.*, 1:22-26. 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, 32:10-14; *see also id.*, 42:10-43:10; MARA-1003, ¶273. Similarly, Wang also discloses extracted microbial lipids, which are “isolated from...microbes.” MARA-1006, [0021]; MARA-1003, ¶¶274-275.

As discussed above, a PHOSITA would have understood Radianingtyas’s teachings directed to an “oil” to be referring to a “lipid,” as these terms are used

interchangeably in the art. MARA-1003, ¶¶274-275; *see also* MARA-1001, 6:14-15, 12:31-38, 30:45-46, 34:23-33, 38:11-21.

[3a]

Radianingtyas-Wang discloses and/or renders obvious [3a]. MARA-1003, ¶¶277-283. 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.” *Id.*, 32:17-33:5; *id.*, *see also* 89:24-26; MARA-1003, ¶¶282-283.

[3b]

Radianingtyas-Wang discloses and/or renders obvious [3b]. MARA-1003, ¶¶284-288.

As discussed previously (*see* §III.A.2), since [3a] requires a triglyceride fraction of at least about 70 wt.% of the lipid fraction, the DHA content of at least 60 wt.% of such a triglyceride fraction (i.e., 70 wt.% of the lipid fraction) is expressed as the DHA content constituting at least 42 wt.% of the lipid fraction when the triglyceride fraction is 70 wt.% of the lipid fraction. MARA-1003, ¶285.

Radianingtyas discloses a DHA content of at least 42 wt.% of the lipid fraction (i.e., at least 60% by weight of the triglyceride fraction) because it teaches

that microorganisms produce lipid compositions where DHA is present at up to 60 wt.% of the lipid composition (i.e., the lipid fraction). MARA-1007, 26:29-27:3.

Compositions having a DHA content of the triglyceride fraction that is at least 60% by weight were well known to a PHOSITA based on the prior art that was available before the Critical Date. MARA-1003, ¶¶286-287. 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]; MARA-1009, 27; MARA-1032, 27-31; MARA-1015, [0116], Fig. 3. It was also known that no more than routine skill was necessary to increase the yield of desired fatty acids, including DHA. For example, it was known that decreasing agitation or dissolved oxygen would result in increases of DHA. MARA-1007, 28:15-17, 27:13-21. “[I]f 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, ¶¶287-288.

[3c]

Radianingtyas-Wang renders obvious [3c]. MARA-1003, ¶¶289-293.

As discussed above (§§III.C.1-3, *supra*), a PHOSITA would have combined the teachings of Wang to Radianingtyas to yield a better quality oil composition having a reduced anisidine value. MARA-1003, ¶¶290-291. They would have done so for multiple reasons: (1) to improve the quality of the oil, (MARA-1006, [0170]-[0172]; MARA-1013, [0009]); and (2) to produce “stable” products that are able to meet “market realities and the ability to store and transport the product at readily attainable environmental conditions,” (MARA-1007, 6:25-7:2; *see also* MARA-1006, [0170]; MARA-1014, [0032]). MARA-1003, ¶291.

It would have been obvious to a PHOSITA that the proposed combination produces an oil having an anisidine value within the range of 0.5 to 26 because Wang teaches removing and/or reducing compounds from oils to produce a resultant oil composition having an anisidine value of less than 25. MARA-1006, [0070], [0071], [0153]; MARA-1003, ¶¶292-293.

[3d]

Radianingtyas-Wang renders obvious [3d]. MARA-1003, ¶¶294-303.

For the same reasons as discussed above (§III.A.4, *supra*), [3d] is an optional element for which prior art disclosure is not necessary to meet the claim element. *See* §III.A.4; *AC Techs*, 912 F.3d at 1367; MARA-1003, ¶295.

However, even if less than 5 wt.% organic solvent was a necessary element, the combination of Radianingtyas and Wang renders obvious this element. For

example, Radianingtyas describes “carrying out extraction...via supercritical fluid extraction means,” which uses small amounts or no organic solvent. MARA-1007, 32:10-16. It would have been obvious to a PHOSITA that using supercritical fluid extraction with supercritical CO₂ as the solvent would yield a composition having less than 5 wt.% organic solvent in the extracted microbial lipid simply because very little or no organic solvent is used. MARA-1007, 45:7-9; MARA-1003, ¶296. A PHOSITA would have been motivated to apply a supercritical fluid extraction means using carbon dioxide instead of an organic solvent for multiple reasons, including those described below.

First, a PHOSITA would have been motivated to use supercritical fluid extraction with carbon dioxide as a solvent to avoid problems that “exist with conventional methods utilized for oil recovery from biomass” in that “conventional methods include organic solvent extraction...which can present ecological problems[.]” MARA-1016, 2:24-29; MARA-1003, ¶297.

Second, a PHOSITA would have been motivated to use supercritical fluid extraction with carbon dioxide as a solvent to avoid “[o]ther problems concern[ing] product recovery, as natural oils such as PUFAs are susceptible to thermal and oxidative degradation under the harsh conditions these techniques employ.” MARA-1016, 2:29-32; MARA-1003, ¶298.

Third, a PHOSITA would have been motivated to use supercritical fluid

extraction with carbon dioxide as a solvent because “oils for human consumption should be obtained using methods that employ solvents that are acceptable in terms of toxicity, handling, safety and cost.” MARA-1016, 2:32-34; MARA-1003, ¶299.

Fourth, a PHOSITA would have been motivated to use supercritical fluid extraction with carbon dioxide as a solvent to because doing so would have amounted to nothing more than the use of a known technique (e.g., using supercritical fluid extraction) to improve similar oils according to known methods (e.g., extracting and refining microbial oils) to yield predictable results (e.g., resultant oil having less residual organic solvent). *KSR*, 550 U.S. at 417; MARA-1003, ¶300.

Although Radianingtyas further discloses an alternative method of extraction that involves “extraction with a solvent such as chloroform, hexane, methanol, [or] ethanol,” a PHOSITA would have found Radianingtyas’s disclosure of using “supercritical fluid extraction means” to be an obvious design choice considering that it is one of only *two* presented options for extraction. MARA-1007, 32:10-14 (“extraction with a solvent...or via supercritical fluid extraction mean.”); *see also id.*, 42:10-25; *Kuhle*, 526 F.2d at 555.

And even if an organic solvent was introduced during extraction, methods for reducing and removing organic solvents present in an oil composition (e.g., refining methods) were readily known to a PHOSITA prior to the Critical Date.

MARA-1007, 42:19-25; MARA-1003 ¶¶301-302. Indeed, Radianingtyas explicitly teaches removal of impurities, such as solvents, via filtration, centrifugation or settling, or evaporation. MARA-1007, 42:26-43:10, 104:23. A PHOSITA would have understood that residual organic solvents from extracting microbial oils were not preferred and would have naturally looked to remove them from the resulting composition. MARA-1003 ¶¶302-303; MARA-1016, 2:24-34.

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.*, 8. “Previously presented art includes art made of record by the Examiner, and art provided to the Office by an applicant, such as on an Information Disclosure Statement (IDS), in the prosecution history of the challenged patent.” *Id.*, 7-8. Here, the previously presented art includes Bijl as well as Schaap, whose European counterpart appears on the face of the ’578 patent. MARA-1001. While the United States publication of Schaap does not appear there, its disclosure is the same. Notably, neither Schaap nor Bijl were cited in a

rejection or discussed substantively during prosecution.

Patent Owner may argue that the remaining art presented in this Petition is substantially the same art or presents the same arguments. Petitioner respectfully disagrees. None of Wang, Kralovec, Radianingtyas, Komazawa, or Nichols-I were before the Examiner; none was cited during prosecution; and all fully disclose background teachings that were not discussed by the Examiner during prosecution. For example, the first art the Examiner cited, Dueppen in view of Metz, did not disclose microbial oils in triglyceride fractions but instead winterized oils in solid fractions. And the second art cited by the Examiner, Apt and Elswyk, did not speak to limitations such as solvent or anisidine value but instead were silent on the matter.

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 repeatedly amended its claims.

For example, the Petition highlights that the art cited in this Petition discloses elements directly responsive to claim amendments. In 2019, the Examiner allowed the patent after consideration of both Apt (U.S. Patent No. 8,207,363) and Elswyk, U.S. Pub. 2003/0060509. This is because Applicants amended their claims to recite an anisidine value range of 0.5 to 26 and argued that neither Apt nor Elswyk "teach or suggest a composition having such an anisidine value." MARA-1002, 1073. The Examiner, however, should have looked for other art in light of Applicant's further statement that "Claims 52-54 are directed to extracted microbial oils, wherein the extraction process produces lower anisidine values than other extraction processes." *Id.* But no rejection to any other art

encompassing extracted oils followed.

The Examiner's failure to consider Schaap, Wang, and Bijl—in addition to Nichols-I, Komazawa, Kralovec, and Radianingtyas—is dispositive. Schaap, Wang, and Bijl explicitly disclose oils with anisidine values under 25. Each further discloses that anisidine values under 25 were an inherent property of extracted oils from microbial sources. 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, ¶¶61-62. 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.

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

Mara provides the following designation of counsel.

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D. Service Information

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

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Respectfully submitted,

Dated July 14, 2023

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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 13,953 words, which is less than the 14,000 allowed under 37 CFR § 42.24.

Dated July 14, 2023

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CERTIFICATE OF SERVICE

Pursuant to 37 CFR §§ 42.6(e)(4)(i) *et seq.* and 42.105(b), the undersigned certifies that on July 14, 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:

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