

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MARA RENEWABLES CORPORATION,
Petitioner,

v.

DSM IP ASSETS, B.V.,
Patent Owner.

IPR2023-01342
Patent 10,757,959 B2

Before SUSAN L. C. MITCHELL, ZHENYU YANG, and
JON B. TORNQUIST, *Administrative Patent Judges*.

TORNQUIST, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

Mara Renewables Corporation (“Petitioner”) filed a Petition requesting *inter partes* review of claims 1–14 of U.S. Patent No. 10,757,959 B2 (Ex. 1001, “the ’959 patent”). Paper 2 (“Pet.”). DSM IP Assets, B.V. (“Patent Owner”) filed a Preliminary Response to the Petition. Paper 7.

An *inter partes* review may not be instituted “unless . . . the information presented in the petition . . . shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a) (2018).

Having considered the arguments and evidence presented by Petitioner and Patent Owner, we determine that Petitioner has not demonstrated a reasonable likelihood of prevailing on at least one of the challenged claims of the ’959 patent. Accordingly, we deny institution of an *inter partes* review.

II. BACKGROUND

A. Related Matters

The parties indicate that they are not aware of any judicial or administrative matter that would affect, or be affected by, a decision in this matter. Pet. 72; Paper 5, 1.

B. Real Parties-in-Interest

Petitioner identifies itself and Algal Omega 3 Ltd. as the real parties-in-interest. Pet. 72. Patent Owner identifies itself as the real party-in-interest. Paper 5, 1.

C. The ’959 patent and Related Technology

The ’959 patent “is directed to isolated thraustochytrid microorganisms” and to thraustochytrid biomasses and microbial oils.

Ex. 1001, 1:27–32. The '959 patent explains that the disclosed microorganisms can produce omega-3 fatty acids, which are biologically important molecules that affect cellular physiology, regulate production and gene expression of biologically active compounds, and serve as biosynthetic substrates. *Id.* at 1:63–67, 2:34–37.

Polyunsaturated fatty acids (“PUFAs”) are classified based on the position of the first double bond from the methyl end of the fatty acid. *Id.* at 1:47–49. “[O]mega-3 (n-3) fatty acids contain a first double bond at the third carbon, while omega-6 (n-6) fatty acids contain a first double bond at the sixth carbon.” *Id.* at 1:49–51. Docosahexaenoic acid, or DHA, “is an omega-3 long chain polyunsaturated fatty acid (LC-PUFA) with a chain length of 22 carbons and 6 double bonds, often designated ‘22:6 n-3.’” *Id.* at 1:51–55. “Other omega-3 LC-PUFAs include eicosapentaenoic acid (“EPA”), designated as ‘20:5 n-3,’ and omega-3 docosapentaenoic acid (“DPA n-3”), designated as ‘22:5 n-3.’” *Id.* at 1:55–58. “Omega-6 LC-PUFAs include arachidonic acid (“ARA”)¹, designated as ‘20:4 n-6,’ and omega-6 docosapentaenoic acid (“DPA n-6”), designated as ‘22:5 n-6.’” *Id.* at 1:59–62.

The '959 patent reports that flaxseed oil and fish oils are known sources of omega-3 fatty acids, but both sources were known to have drawbacks. *Id.* at 2:19–32. In particular, flaxseed oil was known to produce linolenic acid but not many of the other important omega-3 fatty acids, and

¹ Arachidonic acid is identified in the '959 patent as ARA and in the recited prior art as AA or 20:4. Ex. 1001:59–62; Pet. 32; Prelim. Resp. 6 (noting that arachidonic acid is referred to as ARA or 20:4); Ex. 1007, 99:31; Ex. 1009, Table 1. We use these different abbreviations and numerical identifiers interchangeably.

fish oils carry the risk of containing environmental contaminants. *Id.* at 2:19–32. The ’959 patent notes that thraustochytrids have been recognized as an alternative source of omega-3 fatty acids, including DHA, and often “have simpler polyunsaturated fatty acid profiles than corresponding fish or microalgal oils.” *Id.* at 2:34–40. The ’959 patent further notes that strains of thraustochytrid species produce omega-3 fatty acids as a high percentage of the total fatty acids produced by the organisms, but some “isolated thraustochytrids vary in the identity and amounts of LC-PUFAs produced,” and some strains “can have undesirable levels of omega-6 fatty acids and/or can demonstrate low productivity in culture.” *Id.* at 2:40–50. “As such, a continuing need exists for the isolation of thraustochytrids demonstrating high productivity and desirable LC-PUFA profiles.” *Id.* at 2:50–52.

D. Illustrative Claims

Claim 1, reproduced below, is the only independent claim of the ’959 patent and is illustrative of the challenged claims.

1. A microbial oil comprising a triglyceride fraction of at least 70% by weight, wherein the docosahexaenoic acid content of the triglyceride fraction is at least 45% by weight, and wherein the oil comprises 1.5% by weight or less of arachidonic acid.

Ex. 1001, 61:15–19.

E. Asserted Grounds of Unpatentability

Petitioner asserts the following grounds of unpatentability (Pet. 1–2):²

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1	102	Radianingtyas ³
1–14	103	Radianingtyas, Kralovec ⁴
1–14	103	Bijl ⁵ , Nichols-I ⁶ , Kralovec
1–4, 6–14	103	Bijl, Komazawa ⁷

III. ANALYSIS

A. Legal Standard

A claim may be invalid as anticipated if “each and every limitation is found either expressly or inherently in a single prior art reference.” *Sanofi–Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1375 (Fed. Cir. 2006) (internal quotation marks omitted). Anticipation under § 102 may be established by

² The relevant sections of the Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112–29, took effect on March 16, 2013. The ’959 patent issued September 1, 2010 and claims priority to a series of divisional applications, the earliest of which was filed March 19, 2009. Ex. 1001, codes (45), (62). At this stage of the proceeding, neither party disputes that the pre-AIA versions of §§ 102 and 103 apply. *See, e.g.*, Pet. 2; Prelim. Resp. 14.

³ WO 2008/129358 A2, published October 30, 2008. Ex. 1007 (“Radianingtyas”).

⁴ WO 2009/040676 A2, published April 2, 2009. Ex. 1030 (“Kralovec”).

⁵ WO 97/37032, published October 9, 1997. Ex. 1008 (“Bijl”).

⁶ Nichols, et. al., *New Australian Single Cell and Crop Plant Sources of Health-Enhancing Long-Chain Omega-3 Oils*, 13 *Australasian Biotechnology* 26–28, October/November 2003. Ex. 1009 (“Nichols-I”).

⁷ US 2004/0161831 A1, published August 19, 2004. Ex. 1015 (“Komazawa”).

showing, as a matter of fact, that all elements arranged as specified in a claim are disclosed within the four corners of a reference, either expressly or inherently, in a manner enabling one skilled in the art to practice an embodiment of the claimed invention without undue experimentation. *See ClearValue, Inc. v. Pearl River Polymers, Inc.*, 668 F.3d 1340, 1344 (Fed. Cir. 2012).

A patent claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the claimed subject matter and “the prior art are such that the subject matter, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) when in evidence, objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

B. Level of Ordinary Skill in the Art

In order to determine whether an invention would have been obvious at the time the application was filed, we consider the level of ordinary skill in the pertinent art. *Graham*, 383 U.S. at 17. In assessing the level of ordinary skill in the art, various factors may be considered, including the “type of problems encountered in the art; prior art solutions to those problems; rapidity with which innovations are made; sophistication of the

technology; and educational level of active workers in the field.” *In re GPAC, Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995) (quotation omitted).

Petitioner contends that, as of the earliest claimed priority date of the '959 patent, an ordinarily skilled artisan “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.” Pet. 6 (citing Ex. 1003 ¶¶ 63–64). Alternatively, Petitioner proposes that an ordinarily skilled artisan “could have also had a Doctorate degree in a relevant academic discipline with one to two years of related work experience in the same discipline.” *Id.* Petitioner argues that an ordinarily skilled artisan “would have been familiar with microbial oils” and “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.* (citing Ex. 1003 ¶¶ 36–48, 64).

Patent Owner does not provide a definition of the level of ordinary skill in the art, but “reserves its right to proffer what it contends to be the appropriate level of ordinary skill in the art should the Board institute review.” Prelim. Resp. 15. Patent Owner asserts, however, that a person of ordinary skill in the art would have a detailed understanding of the information provided in its Technology Background section, including “the expected impact of cellular biomass growth characteristics on the proportion of triglycerides and phospholipids produced during a microbial fermentation.” *Id.*

For purposes of this Decision, we adopt Petitioner’s definition of the skill level of an ordinarily skilled artisan as it is consistent with the prior art

of record. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (holding that the prior art itself can reflect the appropriate level of ordinary skill in the art). As to the background knowledge possessed by the ordinarily skilled artisan, we agree that such an artisan would have been aware of methods for culturing and extracting oils from microbial sources, including the impact of growth characteristics on the proportions of triglycerides and phospholipids produced during microbial fermentation. Pet. 6; Prelim. Resp. 15.

C. Claim Construction

In an *inter partes* review proceeding, a patent claim is 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). 37 C.F.R. § 42.100(b) (as amended Oct. 11, 2018). This rule adopts the same claim construction standard used by Article III federal courts, which follow *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (en banc), and its progeny. Under this standard, the words of a claim are generally given their “ordinary and customary meaning,” which is the meaning the term would have to a person of ordinary skill at the time of the invention, in the context of the entire patent including the specification. *See Phillips*, 415 F.3d at 1312–13.

Petitioner contends that all claim terms of the ’959 patent “should be given their plain and ordinary meaning.” Pet. 3.

Patent Owner does not contend that any claim terms require construction. Prelim. Resp. 14–15.

For purposes of this Decision, we determine that no claim terms require express construction. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (quoting *Vivid*

Techs., Inc. v. Am. Sci. & Eng'g, Inc., 200 F.3d 795, 803 (Fed. Cir. 1999) (“[O]nly those terms need be construed that are in controversy, and only to the extent necessary to resolve the controversy.”)).

D. Anticipation by Radianingtyas

Petitioner contends claim 1 is anticipated by Radianingtyas. Pet. 7–12. Patent Owner refutes such contention. Prelim. Resp. 15–25.

1. *Radianingtyas*

Radianingtyas discloses “compositions and methods related to oil producing microbes that can produce unsaturated fatty acids.” Ex. 1007, code (57). In particular, Radianingtyas discloses methods of culturing eukaryotes of the order Thraustochytriales and family Thraustochytriaceae that produce unsaturated fatty acids, “such as DHA, EPA and DPA.” *Id.* at 1:22–31.

Radianingtyas discloses that a collection and screening process was used to identify 68 pure strains from collection sites throughout Atlantic Canada. *Id.* at 99:5–9. “All isolates which grew in liquid medium (54 out of 68), produced major amounts of omega-3 polyunsaturated fatty acid, particularly DHA which comprised between 22 and 80% of the total C20 to C22 content of these cells.” *Id.* at 99:16–18. “Of particular interest” in Radianingtyas “is ONC-T18[,] which produces up to 90% of its C20 to C22 content as DHA which is approximately 35% of the total intracellular fatty acids.” *Id.* at 99:22–24. “In addition to the omega-3 oils produced, approximately 80% of all isolates synthesized the omega-6 PUFAs, arachidonic acid (AA) or docosapentaenoic acids (DPA), at concentrations varying between 1 and 18% and 3 and 7% w/w, respectively.” *Id.* at 99:29–32.

With respect to the triglyceride fraction and omega-3 content of the produced lipids, Radianingtyas explains that:

The eukaryotic microorganism, for example, such as ONC-T18, can produce at least about 30 wt.%, 40 wt.%, 50 wt.%, 60 wt.%, 70% wt.% or 80 wt.% (e.g., about 80 wt.%) of a lipid composition per dried cellular biomass. For example, the oil producing microbe can produce a lipid composition comprising from about 25% to about 40% of an omega-3 fatty acid, such as n-3 DHA, (for example, at least 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55% or 60% by weight), and from about 0% to about 3% of the omega-3 fatty acid, EPA, (for example, at least 1% or 2% by weight) and from about 4% to about 12% of an omega-6 fatty acid, such as n-6 DPA, (for example, at least 4%, 5%, 6%, 7%, 8%, 9%, or 10% by weight).

Id. 26:29–27:3.

2. *Petitioner's Arguments*

a. *A microbial oil comprising a triglyceride fraction of at least 70% by weight*

Petitioner contends that Radianingtyas discloses various microbial oils that comprise triglycerides from “96 to about 100%” of the neutral lipids, which “can be at least 95% by weight of total lipids.” Pet. 9–10 (citing Ex. 1007, 32:17–33:5, 89:24–26; Ex. 1003 ¶ 78). For strain ONC-T18, Petitioner contends Radianingtyas discloses that “[a]nalysis of results shows that the fatty acid component which ONC-T18 produces under heterotrophic fermentation *is almost entirely triglyceride (at least 95%)* in nature.” *Id.* at 10 (quoting Ex. 1007, 89:24–26) (emphasis by Petitioner); Ex. 1003 ¶ 79. Thus, Petitioner concludes that ONC-T18 may produce a microbial oil comprising a triglyceride fraction of at least 70% by weight.

b. wherein the docosahexaenoic acid content of the triglyceride fraction is at least 45% by weight

Petitioner contends that Radianingtyas indicates that its disclosed microorganisms, “such as ONC-T18 . . . can produce a lipid composition comprising from about 25% to about 40% of an omega-3 fatty acid, such as n-3 DHA, (for example, at least . . . 40%, 45%, 50%, 55%, or 60% by weight).” Pet. 10 (quoting Ex. 1007, 26:29–34). According to Petitioner, “[t]he fatty acid component that ONC-T18 produces is ‘at least 95%’ triglyceride, so in an oil containing 60% DHA (as contemplated by Radianingtyas), even if the remaining 5% fatty acid component that was not in triglyceride form was entirely DHA, the oil would still contain 55% DHA in triglyceride form and would still meet” the claim limitation. *Id.* at 10–11 (citing Ex. 1003 ¶¶ 81–84). Finally, Petitioner contends that Radianingtyas teaches that its extracted oils can be further purified to increase DHA content to produce “a final lipid composition [that is] greater than 90% DHA.” *Id.* at 11 (citing Ex. 1007, 8:2–4).

c. wherein the oil comprises 1.5% by weight or less of arachidonic acid

Petitioner contends that Radianingtyas disclose exemplary oils that contain 1.5% by weight or less of arachidonic acid. Pet. 11. Petitioner contends that Example 13 of Radianingtyas demonstrates that approximately 80% of all isolates synthesized arachidonic acid at concentrations varying between 1 and 18%. *Id.* (citing Ex. 1007, 96:1–3, 99:29–32, Fig. 11). As the range of 1 to 18% overlaps the claimed range of 1.5% or less, Petitioner contends the claimed range is anticipated. *Id.* at 11–12. Petitioner further contends that in some embodiments arachidonic acid is found in levels ranging from 0.13% to 0.90% as a percentage of total fatty acid, or in some

embodiments arachidonic acid is not disclosed at all, which means it “is either absent or below the limit of detection.” *Id.* at 12 (citing Ex. 1007, 32:20–25, 34:4–37:14).

3. Analysis

In order to anticipate a claim, a prior art reference “must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements ‘arranged as in the claim.’” *NetMoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1370 (Fed. Cir. 2008) (quoting *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983)). Radianingtyas discloses microbial oils with various levels of DHA and arachidonic acid. There is no disclosure of an individual microbial oil, however, that contains at least 45% DHA and 1.5% or less arachidonic acid by weight as required by claim 1.

With respect to the level of DHA, although Radianingtyas might be interpreted to disclose that some microorganisms can produce up to 60% DHA,⁸ Radianingtyas discloses that the DHA content of ONC-T18 is “typical[ly]” 35% of the total intracellular fatty acids, and in each experiment disclosed in Radianingtyas DHA was produced by ONC-T18 at

⁸ Radianingtyas discloses that “the oil producing microbe can produce a lipid composition comprising from about 25% to about 40% of an omega-3 fatty acid, such as n-3 DHA.” Ex. 1007, 26:31–33. It then gives examples that include 15%, 20%, 45%, 50%, 55%, and 60%, which are outside of the disclosed range. *Id.* at 26:33–34. Dr. Curtis contends the disclosure as a whole should be read as “from about 15% to about 60% of an omega-3 fatty acid, such as n-3 DHA.” Ex. 1003, 39 n.1. Dr. Curtis identifies no microbe in Radianingtyas, however, that is shown to produce more than 40% DHA, and Radianingtyas expressly notes that the typical DHA content produced by ONC-T18 is 35%. Thus, we question Dr. Curtis’ conclusions regarding the DHA content disclosure of Radianingtyas.

levels less than “at least 45%.”⁹ Ex. 1007, 32:21–25 (noting that the “typical composition of fatty acids” produced by ONC-T18 includes 25% DHA), 34:4–37:14 (noting that the control microorganism produced 13.54%, 19.98%, 18.77%, 18.77%, 21.48%, 28.48%, and 14.13% DHA) (Figure 12), 91 (Table 5) (noting that total DHA produced by ONC-T18 was from 24–34.2%), 99:22–24 (“Of particular interest is ONC-T18 which produces up to 90% of its C20 to C22 content as DHA which is approximately 35% of the total intracellular fatty acids.”). Thus, we are not persuaded that Radianingtyas discloses microbial oils produced by ONC-T18 that have a DHA content of “at least 45%.”

As noted by Petitioner, Radianingtyas provides a definition of “purify” and “purifying,” and notes that when these terms are used, it means that a composition could be, for example, 90% pure. Pet. 11; Ex. 1007, 7:26–8:2. As an example of how the term “purified” may be used, Radianingtyas states “[f]or example, if a disclosed eukaryotic microorganism, for example, produces 35% DHA, this could be further ‘purified’ such that the final lipid composition was greater than 90% DHA.” *Id.* at 8:2–4. We are directed to no actual microbial oil in Radianingtyas, however, that was purified to have increased levels of DHA. Rather, Petitioner only proffers what Radianingtyas might say if such an oil existed or had been purified to increase levels of DHA.¹⁰

⁹ Although Radianingtyas discloses the isolation of 68 pure strains, the focus of Radianingtyas is on the production of microbial oil by ONC-T18. Ex. 1007, 2:7–3:28, 99:8–13. Likewise, Petitioner’s arguments relating to levels of DHA and arachidonic acid in Radianingtyas focus on the microbial oil produced by ONC-T18. Pet. 10–12.

¹⁰ Radianingtyas explains elsewhere that it is “very difficult to preferentially

To the extent that ONC-T18 could produce DHA in amounts above the disclosed “typical” levels, or the levels of any example provided in *Radianingtyas*, Petitioner does not demonstrate that such a microbial oil would necessarily have 1.5% by weight or less of arachidonic acid, as recited in claim 1. As noted by Petitioner, 80% of all isolates synthesized arachidonic acid at concentrations varying between 1 and 18%, which suggests that some isolates produced no arachidonic acid and some isolates produced levels of arachidonic acid that are much higher than 1.5%. Petitioner directs us to no persuasive evidence, however, to suggest that the isolates that produced arachidonic acid at levels of 1.5% or less also produced “at least 45% by weight” DHA in the triglyceride fraction. Indeed, as noted by Patent Owner, in each disclosed example of *Radianingtyas* in which arachidonic acid is produced at levels less than 1.5%, DHA is also produced at levels less than 45% by weight. Prelim. Resp. 24 (citing multiple example microbial oils disclosed in *Radianingtyas*). As such, we are not persuaded that *Radianingtyas* discloses every limitation of claim 1, “arranged as in the claim” in “a” microbial oil as required by claim 1. *NetMoneyIn*, 545 F.3d at 1370.

In view of the foregoing, we are not persuaded that Petitioner demonstrates a reasonable likelihood that *Radianingtyas* anticipates claim 1.

separate and purify” desired PUFAs from oils containing more than one PUFA, for example, purifying DHA from an EPA containing oil. Ex. 1007, 14:21–23.

E. Claims 1–14 over Radianingtyas in view of Kralovec

Petitioner contends the subject matter of claims 1–14 would have been obvious over the combined disclosures of Radianingtyas and Kralovec.

Pet. 13–37. Patent Owner refutes such contention. *See* Prelim. Resp. 26–38.

1. *Kralovec*

Kralovec discloses “a process for increasing the concentration of polyunsaturated fatty acid in an oil composition.” Ex. 1030, 1:9–11. Kralovec notes that polyunsaturated fatty acids, such as the omega-3 fatty acids EPA and DHA, have known health benefits. *Id.* at 1:13–17. Kralovec further notes that omega-3 fatty acids in triglyceride form “are often derived from marine oils, microbial, and/or algal oils,” but notes that these sources also provide “other undesired, fatty acids (*e.g.*, saturated fatty acids).” *Id.* at 2:4–8. Thus, Kralovec asserts that “purifying and concentrating PUFA’s in a triglyceride form is generally desired.” *Id.* at 2:7–8.

The disclosed method of Kralovec includes a hydrolysis step utilizing an enzymatic lipase that “removes one or more saturated and/or short chain fatty acids, or esters thereof, from a starting glyceride, thus leaving a glyceride fraction (hydrolyzed glyceride) where glyceride molecules with unsubstituted alcohol groups and/or polyunsaturated fatty acid esters remain.” *Id.* at 8:20–23, 9:8–10; Ex. 1003 ¶ 95. Kralovec explains that “the hydrolysis step removes all or substantially all of any saturated and/or short chain fatty acids from the starting glyceride,” but “does not remove a substantial amount of polyunsaturated fatty acids, if present, from the glyceride.” Ex. 1030, 8:30–32.

After hydrolysis, the hydrolyzed glyceride can be separated from some or all of the free saturated fatty acids. *Id.* at 12:13–21. “After

hydrolysis and separation, desirable polyunsaturated fatty acid components, for example, EPA and/or DHA, can be attached to the hydrolyzed and distilled glyceride using a lipase,” which is referred to as an “esterification step.” *Id.* at 13:26–29, 14:16–17.

2. *Petitioner’s Arguments*

Petitioner contends that one of ordinary skill in the art would have sought to use Radianingtya’s microbial oil with high levels of DHA in view of the many recognized health benefits associated with DHA, and would have sought to use Kralovec’s method to further increase the DHA in the microbial oil that is produced. Pet. 15–17 (citing Ex. 1007, 1:6–8; Ex. 1030, 1:16–2:3, 18:10–19:6, 35:20–32) (“Kralovec provides methods for obtaining compositions containing ‘triglycerides with higher DHA . . . contents than the starting triglycerides.’”). Petitioner further contends that one of ordinary skill in the art would have sought a microbial oil with low levels of arachidonic acid because “a high-purity, DHA-containing oil” that is “free of contaminants or other PUFAs” would provide for “more efficient supplementation of human and animal food products.” *Id.* at 23–24; Ex. 1035, 381 (“Concentrates keep the intake of calories and other possibly physiologically active fatty acids as low as possible.”).

According to Petitioner, applying Kralovec’s purification method to Radianingtya’s extracted microbial oil would “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 increased concentration of a desired PUFA, e.g., DHA).” *Id.* at 19 (citing *KSR*, 550 U.S. at 417).

Petitioner contends the microbial oil of the Radianingtyas/Kralovec combination would have a triglyceride fraction of at least 70%, as both references already disclose these levels, and the DHA content of this triglyceride fraction would be at least 45% by weight, as disclosed in Radianingtyas. Pet. 20–22 (citing Ex. 1003 ¶ 123). Petitioner further contends that one of ordinary skill in the art would have understood that the resulting microbial oil would have 1.5% or less arachidonic acid as Radianingtyas discloses arachidonic acid levels varying between 1 and 18%, “a wide range of oils with consistently low amounts of ARA,” and some embodiments with no detectable ARA at all. *Id.* at 23 (citing Ex. 1007, 34:4–37:14, 96:1–3, 99:29–32, Fig. 11). Petitioner further contends that Kralovec teaches an embodiment using its purification method in which ARA is present at no more than 1.4% of the glyceride fraction. *Id.* (citing Ex. 1030, 43–44; Ex. 1003 ¶ 125).

3. *Analysis – Claim 1*

Radianingtyas reports that it isolated 68 pure strains of the genus *Schizochytrium* and *Thraustochytrium*. Ex. 1007, 99:5–9. Of these isolates, 54 out of 68 grew in liquid medium. *Id.* at 99:16–18. One isolate, ONC-T18, produced DHA as approximately 35% of the total intracellular fatty acids. *Id.* at 99:22–24. Radianingtyas further reports that 80% of all isolates produced arachidonic acid (AA) at concentrations between 1 and 18%. *Id.* at 99:29–33. From this disclosure, we do not know which isolates discussed in Radianingtyas produced arachidonic acid, or at what levels. For example, we do not know if the isolates that produce high levels of DHA also produced high levels of arachidonic acid, or if there are any isolates that produced high levels of DHA and no arachidonic acid.

To the extent Petitioner relies on the microbial oil of ONC-T18, Radianingtyas reports that “the typical composition of fatty acids for ONC-T18” includes myristic acid, pentadecanoic acid, palmitic acid, palmitoleic acid, stearic acid, oleic acid, eicosapentaenoic acid, decosapentaenoic acid, and docosahexaenoic acid. Ex. 1007, 32:17–25. Arachidonic acid is not included in this list of typical fatty acids produced by ONC-T18, but the DHA content is only 25%. *Id.* Petitioner does not demonstrate that Kralovec’s method could increase DHA content in a triglyceride fraction from 25% to 45% or more. Indeed, Table 9.1 shows Kralovec’s method increasing DHA from 22.0% to 34.5%, or roughly 55%, which would not be sufficient to increase the 25% DHA of ONC-T18 to “at least 45% by weight.”

Moreover, in each fermentation example reported in Radianingtyas for ONC-T18, arachidonic acid is present in measurable amounts. *See* Ex. 1007, Table 6, Figs. 11–12 (C20:4w6); *see id.* at 3:15–16 (noting that Figure 11 reports the results of culturing ONC-T18). For example, in Figure 11 the amount of C20:4w6 is reported for both a “control” fermentation and fermentations that add different “fatty acid production antagonist[s].” *Id.* at 33:11–37:14, Fig. 11. In each control and antagonist-containing fermentations reported in Figure 11, arachidonic acid is produced in measurable amounts. *Id.* Thus, we agree with Patent Owner that microbial oils of ONC-T18 that produce DHA would be expected to produce some arachidonic acid. Prelim. Resp. 37–38.

Example 4 of Kralovec provides guidance as to the extent that Kralovec’s concentration method would increase arachidonic acid in a PFUA composition. In this example, a microbial oil was hydrolyzed, the free fatty acid fraction was removed “by molecule distillation,” and

FFA55/16¹¹ was added to the glyceride fraction in combination with a lipase to produce a re-esterified product. Ex. 1030, 42:3–10. Kralovec reports that the arachidonic acid content of the starting microbial oil was 0.9%, the arachidonic acid content of the glyceride fraction was 1.4%, the arachidonic acid content of the free fatty acid fraction was 0.0%, and the arachidonic acid content of the re-esterified product was 2.5%. *Id.* at Table 9.1; Prelim. Resp. 28. Thus, the arachidonic acid content of the microbial oil increased from 0.9% to 2.5%.

Given that each working example of Radianingtyas produced some level of arachidonic acid, and given that Kralovec’s method would increase the level of both DHA and arachidonic acid in the resulting product, Petitioner does not sufficiently demonstrate that the combination of Radianingtyas and Kralovec (using any particular strain disclosed in Radianingtyas) would result in a microbial oil with a triglyceride fraction of at least 70% by weight, a DHA content in the triglyceride fraction that is at least 45% by weight, *and* an arachidonic acid content in the oil that is less than 1.5% by weight. Nor does Petitioner sufficiently explain why one of ordinary skill seeking “low levels of ARA in a primarily DHA-containing oil” would use a method that would *increase* the level of ARA in that oil. Pet. 23. Accordingly, Petitioner has not demonstrated a reasonable likelihood that claim 1 would have been obvious over Radianingtyas and Kralovec.

¹¹ FFA55/16 is a concentrated mixture of EPA/DHA in the form of free fatty acids. Ex. 1030, 40:3–5.

4. *Analysis—Dependent Claims 2–14*

Claims 2–14 all depend, directly or indirectly, from independent claim 1. Petitioner’s arguments with respect to these claims do not remedy the deficiencies noted above with respect to claim 1. Pet. 24–37.

Accordingly, Petitioner has not demonstrated a reasonable likelihood that claims 2–14 would have been obvious over Radianingtyas and Kralovec.

F. Claims 1–14 in view of Bijl, Nichols-I, and Kralovec

Petitioner contends the subject matter of claims 1–14 would have been obvious over the combined disclosures of Bijl, Nichols-I, and Kralovec. Pet. 37–56. Patent Owner refutes such contention. *See* Prelim. Resp. 38–51.

1. *Bijl*

Bijl discloses a pure and stable microbial oil that contains at least one polyunsaturated fatty acid (PUFA). Ex. 1008, 1:8–12. The microbial oil of Bijl is produced by one or more microorganisms, “suitably in a fermentation process,” and “has a triglyceride content of greater than 90%.” *Id.* at 2:30–36.

In the process of Bijl, microbes are fermented to obtain a microbial biomass that is then filtered or otherwise treated to form a biomass cake. *Id.* at 8:7–19. The biomass is then granulated into granular particles, preferably by extrusion. *Id.* at 8:20–22. The PUFA is then extracted from the dried granules using a solvent. *Id.* at 8:36–9:4. According to Bijl, this process “can enable a cost effective and efficient extraction of the PUFA oil, and provide an oil of a particularly high quality.” *Id.* at 9:5–7.

Bijl explains that the microbial oil may be obtained from algae or fungi. *Id.* at 6:3–5. The algae may include dinoflagellates of the genus *Cryptothecodinium* and the “fungus can be of the genus *Mucorales*, e.g.,

Thraustochytrium.” *Id.* at 6:5–7. Bijl also explains that typically “the oils obtained from these organisms predominantly contain one particular polyunsaturated fatty acid,” but may contain other polyunsaturated fatty acids in lesser amounts. *Id.* at 5:24–26, 6:11–14. The polyunsaturated fatty acids that may be present in the microbial oil include DHA and arachidonic acid. *Id.* at 5:30–35.

2. *Nichols-I*

Nichols-I discloses Australian single cell sources of omega-3 long-chain (>C20) polyunsaturated fatty acids (LC-PUFA). Ex. 1009, 26.¹² In particular, Nichols-I discloses the isolation of new strains of Australian thraustochytrids, which produce both high oil and LC-PUFA content. *Id.* at 27. Nichols-I notes that one isolated strain, strain O, “is particularly attractive as it contains very high levels of DHA (61%),” and less than 5% of other individual PUFAs. *Id.* Nichols-I notes that arachidonic acid (AA) represents 0.7% of the fatty acids produced by strain O. *Id.* (Table 2).

3. *Petitioner’s Arguments*

a. *Combination of Bijl and Nichols-I*

Petitioner contends that one of ordinary skill in the art would have sought to use Nichols-I’s thraustochytrids in Bijl because they produce both high oil and LC-PUFA content and can be grown in fermenters with an organic carbon source, rendering them “a highly attractive, renewable and contaminant free, source of omega-3 oils.” Pet. 40–41 (citing Ex. 1009, 27; Ex. 1003 ¶ 200). Petitioner contends one of ordinary skill in the art would have selected strain O in particular for use in Bijl because it “is particularly

¹² Our citations are to the original page numbers of the document.

attractive” due to its “very high levels of DHA (61%),” which was known to be “beneficial against various human disorders.” *Id.* at 41 (quoting Ex. 1009, 26–27). Petitioner further contends that one of ordinary skill in the art would have selected strain O because it “contained only 0.7% ARA,” and Bijl teaches that “degradation is particularly high when the PUFA is ARA.” *Id.* (quoting Ex. 1008, 3:25–27). Finally, Petitioner contends that using strain O as the source for Bijl’s extracted oils would have amounted to nothing more than the use of a known technology, to improve similar oils in the same way, to yield predictable results. *Id.* at 41–42 (citing *KSR*, 550 U.S. at 417).

Petitioner contends one of ordinary skill would have had a reasonable expectation of success in combining Bijl and Nichols-I because Bijl discloses that its processes are compatible with a wide range of microbial sources, including *Thraustochytrium*, and “both teach that the desired product is one of high enough quality for use in the human diet, including in infant formula.” *Id.* at 42 (citing Ex. 1008, 6:3–11, 13:19–31, 14:23–27; Ex. 1009, 27–28; Ex. 1003 ¶ 204).

b. Combination of Bijl and Nichols-I with Kralovec

Petitioner contends that one of ordinary skill in the art would have sought to use Kralovec’s oil modification techniques to increase the DHA content of the microbial oil of Bijl and Nichols-I as this method would both remove undesired fatty acids present in the oil and provide “triglycerides that have better color and lower levels of trans-isomers” that can be “incorporated into food products, nutraceuticals, pharmaceutical formulations, and microcapsules.” Pet. 43–44 (citing Ex. 1030, 35:21–36:2; Ex. 1003 ¶ 208). Petitioner also contends that applying Kralovec’s method

to the microbial oil of Bijl/Nichols-I would “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).” *Id.* at 44 (citing *KSR*, 550 U.S. at 417; Ex. 1003 ¶ 209).

c. Limitations of Claim 1

Petitioner contends the combination of Bijl, Nichols-I, and Kralovec discloses every limitation of claim 1. In particular, Petitioner contends that Bijl discloses a microbial oil with a triglyceride content of greater than 90%, and optionally higher than 97 wt.%, and Kralovec discloses an oil with a triglyceride fraction that is equal to 60%, 70%, 75%, or 80% of the total composition by weight. Pet. 45–46 (citing Ex. 1008, 1:8–11, 2:30–33, 4:24–28; Ex. 1030, 37:22–24). Petitioner further contends that the use of Strain O of Nichols-I in Bijl would yield an improved oil composition having greater than 60 wt.% DHA. *Id.* at 47 (citing Ex. 1009, 27 (noting that strain O contains “very high levels of DHA (61%)”). Petitioner contends that one of ordinary skill in the art would have understood that the microbial oil of Bijl/Nichols-I/Kralovec would contain less than 1.5 wt.% arachidonic acid as Nichols-I discloses that strain O contains 0.7% arachidonic acid and Kralovec discloses that in one embodiment, after processing, the microbial oil contained no more than 1.4% ARA in the glyceride fraction. *Id.* (citing Ex. 1009, 27; Ex. 1030, 43–44).

4. Analysis – Claim 1

Petitioner’s ground relies on the use of Nichols-I’s preferred thraustochytrids in Bijl. Pet. 40–41. Nichols-I discloses microbial oil

compositions produced by four strains of thraustochytrids: strains A, C, H, and O. Ex. 1009, 27 (table 2). Strains A, C, and H produce 4%, 10.5%, and 13.4% arachidonic acid, respectively. Thus, to the extent Petitioner relies on thraustochytrid strains other than strain O in this ground, it has not sufficiently explained why the resulting microbial oil would have 1.5% or less arachidonic acid, as recited in claim 1.

To the extent Petitioner relies on the use of Nichols-I's strain O in Bijl, the prior art indicates that the levels and proportions of PUFAs produced by thraustochytrids may vary based on the culture conditions used. Ex. 1030, 6 (noting that the composition of microbial oil is affected by the reaction conditions); Ex. 1015 ¶ 116; Ex. 1007, 27:13–21 (noting that the composition of lipid produced “can be manipulated based on the growing medium composition the oil producing microbe multiplies in”). Nichols-I does not report the fermentation conditions used for strain O and Petitioner does not persuasively demonstrate that the same levels of DHA and arachidonic acid would be produced by this strain when fermented and processed using the conditions and methods of Bijl.

Moreover, to the extent Bijl's fermentation methods would reproduce the same DHA and arachidonic acid content reported in Nichols-I for strain O, Petitioner has not established that one of ordinary skill in the art would have expected success in modifying the oil of Bijl/Nichols-I using the techniques of Kralovec to obtain an oil with less than 1.5% arachidonic acid, as recited in claim 1. DHA and arachidonic acid are both polyunsaturated fatty acids. Ex. 1001, 1:47–62. Kralovec discloses that its “hydrolysis step removes all or substantially all of any saturated and/or short chain fatty acids from the starting glyceride *and does not remove a substantial amount of polyunsaturated fatty acids*, if present, from the glyceride.” Ex. 1030, 8:29–

32 (emphasis added). Consistent with this disclosure, Kralovec discloses one embodiment wherein a microbial oil containing 0.9% arachidonic acid was hydrolyzed, the saturated and/or short chain fatty acids separated from the glyceride fraction, and the glyceride fraction then re-esterified in the presence of added EPA and DHA to form an oil with reduced levels of short chain fatty acids and saturated fatty acids. Ex. 1030, 43 (Table. 9.1). The arachidonic acid content of the resulting microbial oil was 2.5%, which is above the 1.5% level recited in claim 1. *Id.*

Given that Kralovec's methods would be expected to increase both DHA and arachidonic acid in the re-esterified product, and was known to increase arachidonic acid levels above the level recited in claim 1, we are presented with insufficient reasoning supported by evidence to conclude that the 0.7% arachidonic acid content of strain O would remain at or below 1.5% after the method of Kralovec is applied to the microbial oil of Bijl/Nichols-I. As such, Petitioner has not demonstrated a reasonable likelihood that claim 1 would have been obvious over Bijl, Nichols-I, and Kralovec.

5. Analysis—Claims 2–14

Claims 2–14 all depend, directly or indirectly, from independent claim 1. Petitioner's arguments with respect to these claims do not remedy the deficiencies noted above with respect to claim 1. Pet. 50–56. Accordingly, Petitioner has not demonstrated a reasonable likelihood that claims 2–14 would have been obvious over Bijl, Nichols-I, and Kralovec.

G. Claims 1–4 and 6–14 over Bijl and Komazawa

Petitioner contends the subject matter of claims 1–4 and 6–14 would have been obvious over the combined disclosures of Bijl and Komazawa. Pet. 56–68. Patent Owner refutes this contention. *See* Prelim. Resp. 51–66.

1. *Komazawa*

Komazawa discloses “a novel microorganism having an ability of producing docosahexaenoic acid (DHA) and the use of said microorganism.” Ex. 1015 ¶ 1. In particular, Komazawa discloses a *Thraustochytrium* strain, LFF1, that has the ability to produce DHA. *Id.* ¶¶ 10, 11, 13.

Komazawa notes that the preferred pH of culturing “is 8.0 to 9.0” and the resulting DHA-containing fat and oil contains 10% by weight or less of docosapentaenoic acid and 30% by weight or more of DHA, and preferably “50% by weight or more” of DHA. *Id.* ¶¶ 14–16.

Komazawa discloses a series of examples that report the level of production of “fat and oil” by the LFF1 strain. *Id.* ¶¶ 72–184. In Example 5, the pH of the culture was adjusted to be 4.5, 7.5, or 8.5. *Id.* ¶¶ 115–116. Komazawa reports that the DHA component in the triglycerides “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,” with a DHA yield of 0.8 g/L culture. *Id.* ¶ 116. Komazawa does not report the presence of arachidonic acid in any of its examples. *Id.* ¶ 108, Table I.

2. *Petitioner’s Arguments*

Petitioner contends the combination of Bijl and Komazawa discloses every limitation of claim 1. With respect to the requirement for a “microbial oil comprising a triglyceride fraction of at least 70% by weight,” Petitioner

contends that Bijl discloses a microbial oil “which has a triglyceride content greater than 95 wt.%.” Pet. 62 (citing Ex. 1008. 1:8–11, 2:30–33; 1003 ¶¶ 265–266). Petitioner further contends that one of ordinary skill in the art would have understood that Komazawa contains “predominately triglycerides because Komazawa teaches the use of lipase for triglyceride-specific oils.” *Id.* at 62–63 (citing Ex. 1015 ¶¶ 21, 55; Ex. 1022, 185; Ex. 1003 ¶¶ 270–271).

With respect to DHA content, Petitioner contends that Komazawa discloses that the DHA content in the produced oil may be 50% by weight or more, and reports that in one experiment an oil having a “DHA component *in the triglycerides*” of around 40% was obtained, which rose to “a high content of 80% or more” when culturing was carried out at pH 8.5. *Id.* at 64 (quoting Ex. 1015 ¶ 116, Fig. 3)

With respect to arachidonic acid, Petitioner contends that Komazawa discloses the fatty acid composition of the extracted lipid and does not report the presence of arachidonic acid. *Id.* (citing Ex. 1015 ¶ 112, Table 1 (showing 100% oils with no ARA)). Thus, to the extent any arachidonic acid is present in Komazawa’s oil, Petitioner contends “it is below the limit of detection, which is lower than 1.5% based on the data in Table 1” of Komazawa. *Id.*

3. Analysis—Claim 1

Petitioner’s combination relies on the use of Komazawa’s preferred strain of microorganisms as a microbial source for Bijl’s extracted microbial oil. Pet. 58–59. Assuming that the “fat and oil” of Komazawa represents “predominately triglycerides,” as asserted by Petitioner, we are directed to no evidence as to the actual level of triglycerides produced by the

Thraustochytrium strain of Komazawa, or evidence that an oil with “predominantly triglycerides” would have a triglyceride fraction that is at least 70% by weight.

Bijl suggests that in at least some embodiments the triglyceride fraction may be greater than 90%. Ex. 1008, 2:30–35. The evidence of record, however, indicates that not all microbial oils produced in Bijl will have a triglyceride fraction of at least 70% by weight, much less 90%. For example, Bijl discloses a working example in which DHA is produced from *Cryptothecodinium cohnii* according to Bijl’s disclosed methods. Ex. 1008, 4:10–12, 42:4–43:1 (Example 19). In this example, both the DHA content and triglyceride content of the resulting oil are below the thresholds recited in claim 1, with the recovered oil containing only 67% tri-glycerides and 32.6% DHA. *Id.* at 42:33–36. This indicates that not every microorganism cultured and processed according to the methods of Bijl will produce a microbial oil with a triglyceride fraction of at least 70% by weight, or a DHA content of at least 45% by weight.¹³

In view of the foregoing, Petitioner has not demonstrated that the combination of Bijl and Komazawa would result in a “[m]icrobial oil comprising a triglyceride fraction of at least 70% by weight, wherein the docosahexaenoic acid content of the triglyceride fraction is at least 45% by weight,” as recited in claim 1. Accordingly, Petitioner does not demonstrate a reasonable likelihood that claim 1 would have been obvious over the combined disclosures of Bijl and Komazawa.

¹³ Consistent with Bijl’s disclosure that triglycerides may be greater than 90% in some embodiments, in Example 16 of Bijl, an oil produced by *Mortierella alpina* was found to contain 93% tri-glycerides when extracted with hexane. Ex. 1008, 38:17–40:10.

4. *Analysis—Claims 2–4 and 6–14*

Claims 2–4 and 6–14 all depend, directly or indirectly, from independent claim 1. Petitioner’s arguments with respect to these claims do not remedy the deficiencies noted above with respect to claim 1. Pet. 65–68. Accordingly, Petitioner has not demonstrated a reasonable likelihood that claims 2–4 and 6–14 would have been obvious over Bijl and Komazawa.

IV. CONCLUSION

For the foregoing reasons, we determine that Petitioner does not demonstrate a reasonable likelihood that it would prevail with respect to at least one of the claims challenged in the Petition. We, therefore, do not institute an *inter partes* review.

V. ORDER

For the foregoing reasons, it is:

ORDERED that, pursuant to 35 U.S.C. § 314(a), the Petition is denied, and no *inter partes* review is instituted.

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