

Filed on behalf of Commonwealth Scientific and Industrial Research Organisation
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH
ORGANISATION,
Petitioner,

v.

BASF PLANT SCIENCE GMBH,
Patent Owner.

U.S. Patent No. 11,260,095

Issued: March 1, 2022

PETITION FOR POST-GRANT REVIEW

PURSUANT TO 35 U.S.C. §§ 321-328 AND C.F.R. § 42.200 *et seq.*

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EXHIBIT LIST

<u>Exhibit No.</u>	<u>Description</u>
1001	Senger et al., U.S. Patent No. 11,260,095, “Modification of Plant Lipids Contains PUFAs,” issued March 1, 2022
1002	Declaration of Narendra Yadav, Ph. D., in Support of Petition for Post-Grant Review of U.S. Patent No. 11,260,095
1003	Senger et al., PCT International Application Publication No. WO 2016/075325, published May 19, 2016
1004	U.S. Provisional Application No. 62/234,373, filed September 29, 2015
1005	U.S. Provisional Application No. 62/079,622, filed November 14, 2014
1006	Meyer et al. (2003). Biosynthesis of docosahexaenoic acid in <i>Euglena gracilis</i> : biochemical and molecular evidence for the involvement of a $\Delta 4$ -fatty acyl group desaturase. <i>Biochemistry</i> , 42(32), 9779-9788.
1007	File History of U.S. Application No. 15/526,162 excluding copies of references submitted with Information Disclosure Statements
1008	PCT International Patent Application Publication No. WO 2013/153404, published October 17, 2013
1009	Truksa et al., “Molecular analysis of flax 2S storage protein conlinin and seed specific activity of its promoter,” <i>Plant Physiology and Biochemistry</i> , 41 (2003) 141-147
1010	James et al. (1995). Directed tagging of the Arabidopsis FATTY ACID ELONGATION1 (FAE1) gene with the maize transposon activator. <i>The Plant Cell</i> , 7(3), 309-319.
1011	Lassner et al. (1996). A jojoba beta-Ketoacyl-CoA synthase cDNA complements the canola fatty acid elongation mutation in transgenic plants. <i>The Plant Cell</i> , 8(2), 281-292.

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<u>Exhibit No.</u>	<u>Description</u>
1012	Barret et al. (1998). A rapeseed FAE1 gene is linked to the E1 locus associated with variation in the content of erucic acid. <i>Theoretical and Applied Genetics</i> , 96(2), 177-186.
1013	PCT International Patent Application Publication No. WO 2013/185184, published December 19, 2013
1014	PCT International Patent Application Publication No. WO 2015/089587, published June 25, 2015
1015	Rossak, et al. (2001). Expression of the FAE1 gene and FAE1 promoter activity in developing seeds of <i>Arabidopsis thaliana</i> . <i>Plant Molecular Biology</i> , 46(6), 717-725.

I. INTRODUCTION

Commonwealth Scientific and Industrial Research Organisation (“CSIRO”) respectfully requests institution of a post-grant review (“PGR”) of claims 1-11 of U.S. Patent No. 11,260,095 (“the ‘095 Patent,” Ex. 1001) pursuant to 35 U.S.C. §§ 321-329 and 37 C.F.R. § 42.200 *et seq.* This Petition, supported by the accompanying Declaration of Dr. Narendra Yadav (“Yadav Declaration,” Ex. 1002) demonstrates that claims 1-11 of the ‘095 Patent are not patentable.

The ‘095 Patent issued from U.S. Application No. 15/526,162 (“the ‘162 application”), filed on May 11, 2017 as a §371 national stage entry of PCT International Application No. PCT/EP2015/076630 (“the ‘630 application”). PCT International Application No. PCT/EP2015/076630 (Ex. 1003) was filed November 13, 2015 and claims priority to U.S. Provisional Application No. 62/234,373 (“the ‘373 application,” Ex. 1004), filed September 29, 2015 and U.S. Provisional Application No. 62/079,622 (“the ‘622 application,” Ex. 1005), filed November 14, 2014.¹

Claims 1 and 5-8 of the ‘095 Patent recite a *Brassica napus* plant or part thereof, comprising seeds that comprise lipids including eicosapentaenoic acid

¹ Collectively, the applications to which the ‘095 Patent claims priority are referred to herein as the “priority applications.”

(EPA) and docosahexaenoic acid (DHA) and optionally arachidonic acid (ARA), wherein (a) the content of EPA is at least 5% higher than of ARA, (b) the sum of contents of EPA+DHA is at least 7% higher than ARA, and/or (c) the content of ARA is less than 4% and the content of EPA is more than 7% and the content of DHA is more than 2%. These claims further require that the *Brassica napus* plant or part thereof comprises a “Delta-5 elongase gene under the control of a FAE promoter.” Ex. 1002, ¶17.

Claims 2-4 recite a method of altering plant seed lipids composition comprising the step of growing a *Brassica napus* plant according to claim 1 to produce seeds that comprise lipids including EPA, DHA and ARA, wherein the step of growing and lipids production is continued until the content of ARA in the lipids of the seeds has decreased. Ex. 1002, ¶18.

Claims 9-11 of the ‘095 Patent recite a *Brassica napus* plant comprising seeds that comprise lipids including eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and arachidonic acid (ARA), wherein when the *Brassica napus* plant or part thereof is grown, the content of ARA in the lipids of the seeds decreases at least 0.5% by weight of total lipids and the content of EPA and/or DHA in the lipids of the seeds increases. Claims 9-11 also require that the seeds comprise a “Delta-5 elongase under the control of a FAE promoter.” Ex. 1002, ¶19.

The specification of the ‘095 Patent provides neither written description nor enablement for the scope of patent protection it seeks to cover by its claims 1-11. Ex. 1002, ¶20-22.

First, all claims of the ‘095 Patent require the presence of a Delta-5 elongase gene under the control of a “FAE promoter.”² Despite this requirement, the specification of the ‘095 Patent is completely devoid of *any mention* of a “FAE promoter,” much less a Delta-5 elongase gene under the control of a purported FAE promoter. The components of genetic constructs used to generate the transgenic plants of the ‘095 Patent are *not described* in the specification except by reference to the two provisional patent applications to which the ‘095 claims priority. These genetic constructs employ a Delta-5 elongase from *Ostreococcus tauri* under the control of a promoter from the specific FAE1.1 gene from *Brassica napus*. Disclosure found solely in the provisional applications cannot be relied upon to support written description of the claims. *See* 37 CFR 1.57(d). Further, an example of a specific promoter in the provisional applications without any further description cannot provide written description or enablement of a purported class of “FAE promoter” as claimed. Ex. 1002, ¶24.

² The terms “FAE” or “FAE promoter” are not defined in the ‘095 Patent. As discussed in section VI.A, “FAE” could be an abbreviation for “fatty acid elongase.”

Second, the specification of the '095 Patent provides neither written description nor enablement for the full scope of the levels of ARA, EPA, and DHA recited in the claims. The claims recite seeds comprising lipids with a content of ARA that is "less than 4%" with no recited lower limit, yet the seeds with the lowest level of ARA disclosed in the specification had an ARA content of 2.54%. Similarly, the claims recite seeds comprising lipids with a content of EPA that "is more than 7%," and a content of DHA that "is more than 2%" with no recited upper limit, yet the seeds with the highest levels of EPA and DHA disclosed in the specification had an EPA and DHA content of 8.57% and 3.61%, respectively. Based on these disclosures, a person of ordinary skill in the art (POSITA) would understand that (1) the inventors of the '095 Patent were not in possession of the full scope of the claimed invention, and (2) the '095 Patent does not provide enablement across the full scope of the claimed invention. Ex. 1002, ¶25.

Third, the specification of the '095 Patent attributes the levels of ARA, EPA, and DHA recited in the claims to "a Delta-5 elongase gene under the control of a promoter such that expression of the Delta-5 elongase gene is maintained or increased in late stage seed development" (Ex. 1001, at 7:19-23) *not* to "a Delta-5 elongase gene under the control of a *F_{AE} promoter*" as recited in the claims. Indeed, data in the specification show that a FAE promoter *does not* necessarily cause expression of the Delta-5 elongase gene to be "maintained or increased in late stage

seed development” and ***does not*** necessarily result in the claimed levels of ARA, EPA, and DHA. ***All*** plants analyzed in the ‘095 Patent contained a Delta-5 elongase gene under the control of a specific *Brassica napus* FAE1.1 promoter, including those where expression of the Delta-5 elongase gene was not maintained or increased in late stage seed development and where the claimed levels of ARA, EPA, and DHA were not reached. Accordingly, the claimed levels of ARA, EPA, and DHA ***cannot*** be explained by the presence of a “a Delta-5 elongase gene under the control of a ***FAE promoter.***” Ex. 1002, ¶26.

Finally, the claims of the ‘095 Patent are anticipated by PCT International Patent Application Publication Nos. WO 2013/185184 and WO 2015/089587 as detailed herein. Ex. 1002, ¶27.

Accordingly, Petitioner requests institution of a PGR and cancellation of claims 1-11 of the ‘095 Patent.

II. 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)

Pursuant to 37 C.F.R. § 42.8 (b)(1), the real party-in-interest for this Petition is Commonwealth Scientific and Industrial Research Organisation (“CSIRO”), a Government Agency organized under the laws of Australia, having a place of business at CSIRO Black Mountain Science and Innovation Park, Clunies Ross Street, Acton ACT 2601, Australia.

1. Related parties

For the sake of transparency, Petitioner advises the Board that the following parties are commercial partners of CSIRO, and co-owners with CSIRO of some of their own patents in the field of polyunsaturated ω 3-fatty acids:

1. Grains Research and Development Corporation (“GRDC”), an Australian statutory corporation with its principal place of business located at Level 4, East Building, 4 National Circuit, Barton ACT 2600, Australia.
2. Nuseed Nutritional Australia Pty Ltd., an Australian proprietary limited company with its principal place of business at 103–105 Pipe Road, Laverton, North Victoria, 3026, Australia.

Further:

3. Nufarm Limited, located at 103-105 Pipe Road Laverton North Victoria 3026, Australia, is the parent company of Nuseed Pty. Ltd and Nuseed Nutritional Australia Pty Ltd.
4. Nufarm Limited is also the parent company of Nuseed Americas Inc., which is located at 1000 Burr Ridge Pkwy, Burr Ridge, IL 60527, and Nuseed Nutritional US Inc., located at 990 Riverside Parkway, West Sacramento, CA 95605.

None of these related parties are controlling or otherwise have an opportunity to direct or control this Petition or Petitioner's participation in any resulting PGR.

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

Pursuant to 37 C.F.R. § 42.8(b)(2), Petitioner identifies the following judicial or administrative matters that could be affected by a decision in this proceeding:

1. Continuation applications

There is at least one continuation application of U.S. Application No. 15/526,162, from which the '095 Patent issued: U.S. Application No. 17/682,694, filed on February 28, 2022, which is currently pending.

2. Disputes between the parties

The Petitioner and related parties have been involved in the following judicial and administrative proceedings relating to patents in the field of ω -3 polyunsaturated

fatty acid synthesis. These judicial and administrative matters will **not** be affected by a decision in this proceeding:

1. BASF PLANT SCIENCE, LP v. NUSEED AMERICAS, in the United States District Court for the District of Delaware, Civil Action No. :17-cv-00421-VAC-CJB;
2. BASF Plant Science, LP et al. v. Commonwealth Scientific and Industrial Research Organisation et al., in the United States District Court for the Eastern District of Virginia Norfolk Division, Civil Action No. 2:17-cv-00503-HCM-LRL;
3. BASF Plant Science, LP v. Commonwealth Scientific and Industrial Research Organisation / Commonwealth Scientific and Industrial Research Organisation, et al., v. BASF Plant Science, LP, et al., in the United States Court of Appeals for the Federal Circuit, Appeal Nos. 2020-1415, 2020-1416;
4. Post-Grant Review of U.S. Patent No. 10,301,638 B2, assigned to BASF Plant Science GmbH, PGR2020-00033;
5. Post-Grant Review of U.S. Patent No. 10,351,870 B2, assigned to BASF Plant Science GmbH, PGR2020-00057; and
6. Post-Grant Review of U.S. Patent No. 10,533,183 B2, assigned to BASF Plant Science GmbH, PGR2021-00004.

7. Post-Grant Review of U.S. Patent No. 11,180,769 B2, assigned to
BASF Plant Science GmbH, PGR2022-00026.

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

Pursuant to 37 C.F.R. § 42.8(b)(3), lead counsel, first back-up counsel and second back-up counsel for this Petition are Gary J. Gershik (Reg. No. 39,992), Darren Haber (Reg. No. 80,964), and Brian A. Comack (Reg. No. 45,343), respectively. Pursuant to 37 C.F.R. § 42.10(b), Petitioner has filed a power of attorney designating the above-identified counsel.

D. Service Information Under 37 C.F.R. § 42.8(b)(4)

Pursuant to 37 C.F.R. § 42.8(b)(4) service information for the Petition is as follows:

Gary J. Gershik Amster Rothstein & Ebenstein LLP 90 Park Avenue, 21 st Floor New York, NY 10016 Tel: 212-336-8063 Fax: 212-336-8001 Email: ggershik@arelaw.com Email: docketing@arelaw.com	Darren Haber Amster Rothstein & Ebenstein LLP 90 Park Avenue, 21 st Floor New York, NY 10016 Tel: 212-336-8000 Fax: 212-336-8001 Email: dhaber@arelaw.com
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III. ADDITIONAL REQUIREMENTS

A. Payment of fees under 37 C.F.R. § 42.15

Petitioner submits herewith the required fees in accordance with 37 C.F.R. §§ 42.203(a) and 42.15(a). If any additional fees are due during this proceeding, the Office is authorized to charge such fees to Deposit Account No. 01-1785.

B. Timing under 37 C.F.R. § 42.202

The ‘095 Patent issued on March 1, 2022. Pursuant to 37 C.F.R. § 42.202(a), a petition for PGR of a patent must be filed no later than the date that is nine months after the issued date of the patent. Accordingly, the deadline to file a petition for PGR of the ‘095 Patent is December 1, 2022, and this Petition is being timely filed.

C. Grounds for standing under 37 C.F.R. § 42.204(a)

Petitioner hereby certifies that the ‘095 Patent is available for PGR and that Petitioner is not barred or estopped from requesting PGR of any claim of the ‘095 Patent.

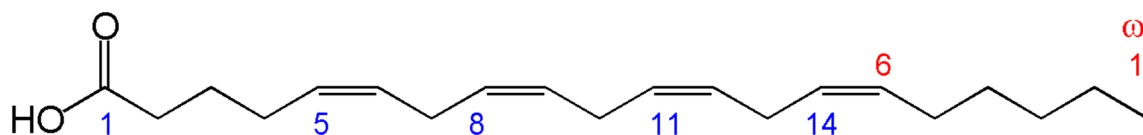
IV. TECHNOLOGY BACKGROUND

The '095 Patent relates, generally, to the production of transgenic plants that produce docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), and optionally Arachidonic Acid (ARA). DHA, EPA, and ARA are fatty acids that are not naturally produced in most plant species. Thus, the '095 Patent describes genetic constructs which are designed to express polypeptides with various enzymatic activities that result in the production of ARA, EPA, DHA. Ex. 1002, ¶28.

A. Docosahexaenoic Acid (DHA), Eicosapentaenoic Acid (EPA), and Arachidonic Acid (ARA)

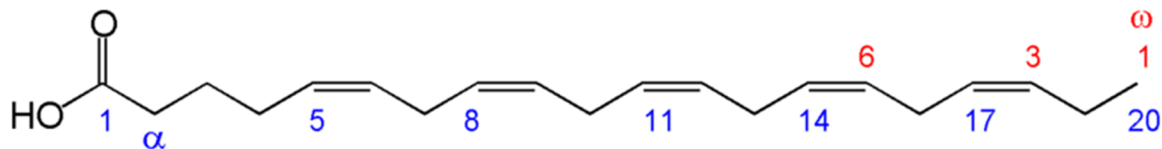
Claims 1-11 of the '095 Patent recite the production of transgenic plants that produce EPA, DHA, and optionally ARA. Ex. 1002, ¶29.

The chemical structure of ARA is:



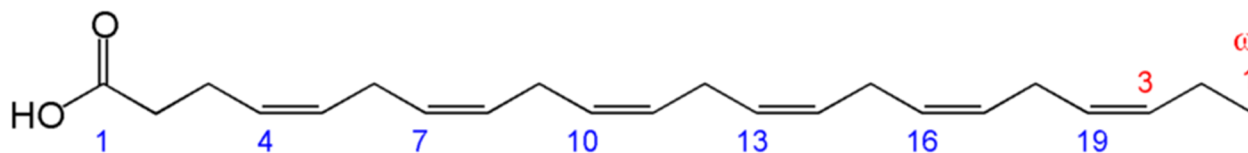
Ex. 1002, ¶30.

The chemical structure of EPA is:



Ex. 1002, ¶31.

The chemical structure of DHA is:



Ex. 1002, ¶32.

The position of the carbon atoms in the backbone of a fatty acid can be indicated by numbering them, either from the carboxyl end or from the methyl end of the carbon chain. Counted from the carboxyl end, it is represented by the Δx , with $x=1, 2, 3$, etc. (numbers under the carbon chain in the diagram). If the position is counted from the methyl end, then it is represented by the ω - x notation (numbers above the carbon chain in the diagram). Ex. 1002, ¶33.

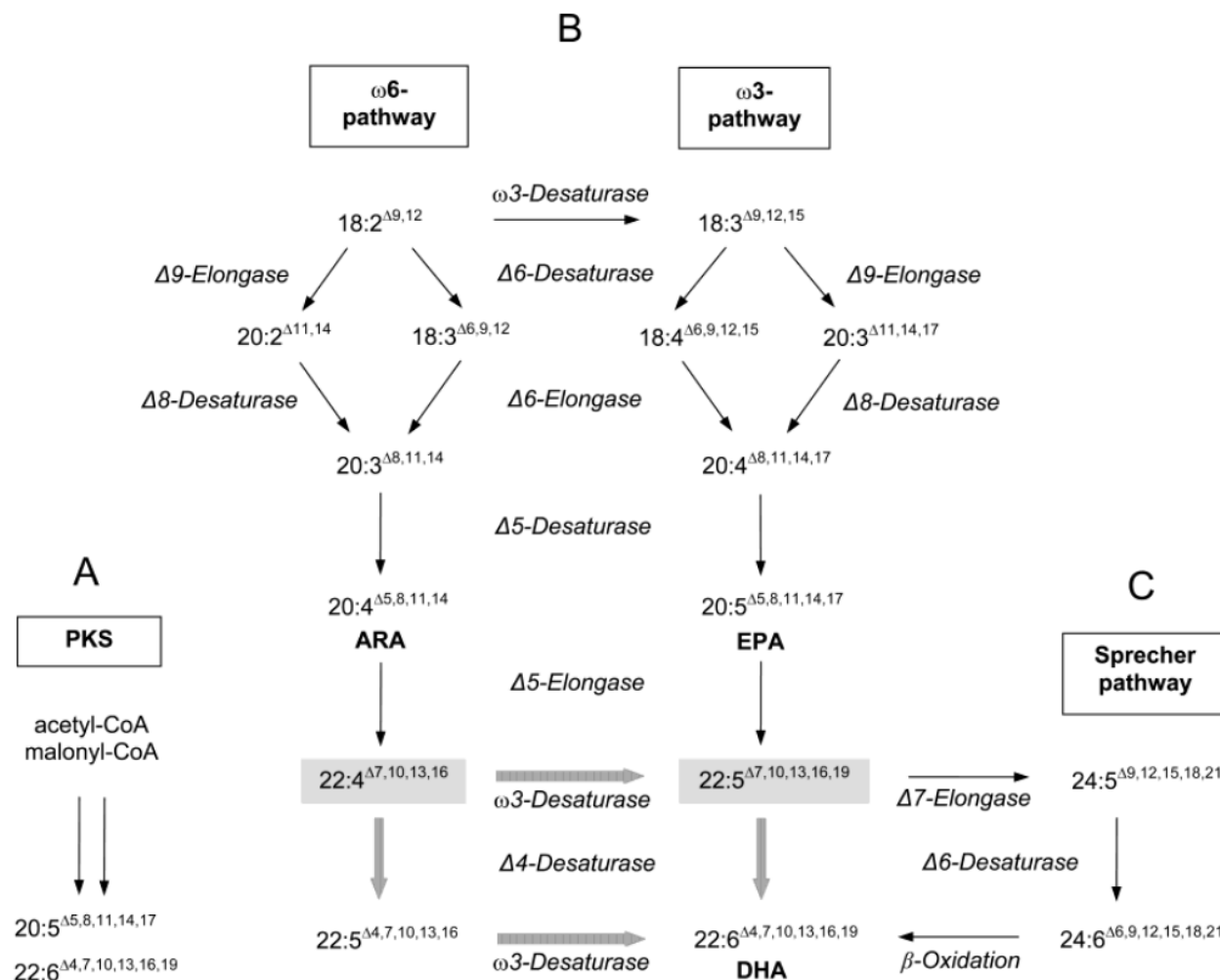
When “ ω - x ” notation is used, only the position of the double bond which is closest to the methyl end is indicated, even if multiple double bonds exist and the 20-carbon fatty acid (EPA) shown in the diagram is named “20:5 ω -3” or “20:5n-3.” Accordingly, any PUFA that has its first double bond on the third carbon from the methyl end of the carbon chain is designated as omega-3 (ω -3), whereas a PUFA with its first double bond on the sixth carbon from end of the carbon chain is designated as omega-6 (ω -6). Ex. 1002, ¶34.

Thus, EPA can be represented using Δ notation as 20:5 $\Delta^{5,8,11,14,17}$ or using ω notation as 20:5 ω -3 and DHA can be represented using Δ notation as 22:6 $\Delta^{4,7,10,13,16,19}$ or using ω notation as 22:6 ω -3. Ex. 1002, ¶35.

B. Biosynthesis of EPA and DHA

Although there are multiple pathways for the biosynthesis of EPA and DHA, the '095 Patent describes transgenic plants using enzymes with activity in the *aerobic* biosynthetic pathway. In the aerobic biosynthetic pathway, EPA and DHA are synthesized through alternating steps of “desaturation” (the addition of a double bond/removal of hydrogen atoms) and “elongation” (the addition of two carbon atoms) by desaturase and elongase enzymes, respectively. Ex. 1002, ¶36.

The aerobic biosynthetic pathway for production of EPA and DHA is summarized in Figure 1 of Meyer et al., 42(32) *Biochem.* 9779-88 (2003) (Ex. 1006) which is reproduced below:



Ex. 1006, p. 9780. Ex. 1002, ¶37.

1. Elongases

Elongases are enzymes that lengthen the fatty acid chain by insertion of a two-carbon unit at the carboxyl end of the fatty acid chain.³ Elongases are often referred

³ Four enzymatic activities are thought to be required for each fatty acid elongation step. However, the term “elongase” is used to refer to the condensing enzyme (or β-

to as “ Δx ”-elongase, where the “x” refers to where the first double bond in the fatty acid must be in order for the elongase to be able to act on the substrate. Thus, as summarized above, the $\Delta 5$ elongase recited in the claims may act on substrates that have their first double-bond at the $\Delta 5$ position (i.e. ARA and EPA). Ex. 1002, ¶38.

The claims of the ‘095 Patent specifically recite the presence of a $\Delta 5$ -elongase under the control of an FAE promoter. According to Figure 1, $\Delta 5$ -elongases can act on ARA as a substrate to produce $22:4^{\Delta 7,10,13,16}$ which is known in the art as “Adrenic Acid.” $\Delta 5$ -elongases can also act on EPA as a substrate to produce docosapentaenoic acid (DPA). DPA can then be converted to DHA by a $\Delta 4$ -desaturase if one is present in the plant. Ex. 1002, ¶39.

2. Desaturases

Desaturases are enzymes that add a carbon–carbon double bond into fatty acid chains. Some desaturases introduce double bonds into unsaturated acyl chains between a pre-existing double bond and the carboxyl group of lipid substrates. These desaturases are called “front-end desaturases” and are often referred to as “ Δx ”-desaturase, where “x” is the number of the carbon atom at which the new double bond is created. Other types of desaturase exist, such as $\omega 3$ - or

ketoacyl CoA synthase) because that enzyme determines whether fatty acid elongation happens in a particular cell and which substrate is acted upon.

ω 6-desaturases, which are called “methyl-end desaturases” because they add a double bond between the methyl end of the fatty acid chain and a pre-existing double bond. ω 3 or “omega-3” desaturases may therefore convert ω 6 fatty acids into ω 3 fatty acids by adding a double bond between the methyl end of the fatty acid chain and a pre-existing double bond. Because these desaturases can only *add* a double bond to fatty acid chains, they cannot convert ω 3 into ω 6 fatty acids. Ex. 1002, ¶40.

3. Promoters

Promoters, generally, are DNA sequences to which transcription factors bind to initiate transcription of RNA from DNA downstream of the promoter. Genes in an organism are naturally associated with promoters that help direct appropriate expression of gene. A wide variety of promoters have been discovered and include those that cause expression of a gene ubiquitously, in specific tissues, at specific times during development, or in response to a particular stimulus. Ex. 1002, ¶41.

The claims of the ‘095 Patent recite a “Delta-5 elongase under the control of a FAE promoter.” “FAE promoter” is not recited or defined anywhere in the ‘095 Patent. Nevertheless, as discussed in section VI.A, a POSITA would understand “FAE promoter” to refer to a promoter that is naturally associated with a “Fatty Acid Elongation” (i.e. “FAE”) gene of an organism. Ex. 1002, ¶42.

The *FATTY ACID ELONGATION1* (*FAE1*) gene was first identified in the early 1990s by mutational analysis in *Arabidopsis thaliana* by several research

groups. The FAE1 gene was subsequently isolated and shown to be expressed in seeds of *Arabidopsis*, but not in its leaves. See James et al. (1995), Ex. 1010. Subsequently, the cDNA of a homologous FAE gene was isolated from the seeds of jojoba and the cDNA of two homologous FAE genes were isolated from *Brassica napus*. See Lassner et al. (1996), Ex. 1011 and Barret (1998), Ex. 1012. Ex. 1002, ¶43.

V. SUMMARY OF THE ‘095 PATENT

The ‘095 Patent issued from U.S. Application No. 15/526,162 (“the ‘162 application”), filed on May 11, 2017 as a §371 national stage entry of PCT International Application No. PCT/EP2015/076630 and therefore must have the same specification as PCT/EP2015/076630. See 35 U.S.C. § 371(c)(2). The ‘162 application also claims priority to and incorporates-by-reference each of U.S. Provisional Application No. 62/234,373 (“the ‘373 application,” Ex. 1004), filed September 29, 2015 and U.S. Provisional Application No. 62/079,622 (“the ‘622 application,” Ex. 1005), filed November 14, 2014.

A. The ‘095 Patent

1. The Claims

Independent claim 1 of the ‘095 Patent reads as follows:

1. *Brassica napus* plant or part thereof, comprising seeds that comprise lipids including eicosapentaenoic acid (EPA) and

docosahexaenoic acid (DHA) and optionally arachidonic acid (ARA), wherein

- a) the content of EPA is at least 5% higher than of ARA, and/or
- b) the sum of contents of EPA+DHA is at least 7% higher than ARA and/or
- c) the content of ARA is less than 4% and the content of EPA is more than 7% and the content of DHA is more than 2%, and

wherein the *Brassica napus* plant or part thereof comprises a Delta-5 elongase gene under the control of a FAE promoter.

Ex. 1001, 35:13-26. Ex. 1002, ¶44.

Independent claim 9 of the '095 Patent reads as follows:

9. *Brassica napus* plant comprising seeds that comprise lipids including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and arachidonic acid (ARA), wherein, when the *Brassica napus* plant or part thereof is grown, the content of ARA in the lipids of the seeds decreases at least 0.5% by weight of total lipids and the content of EPA and/or DHA in the lipids of the seeds increases, wherein the seeds comprise a Delta-5 elongase gene under the control of a FAE promoter.

Ex. 1001, 36:23-32. Ex. 1002, ¶45.

2. The Specification

The apparent focus of the '095 Patent is in providing extracted lipid compositions with high levels of EPA relative to ARA, such as where “the content of EPA is at least 5% higher than the content of ARA.” Ex. 1001, 3:15. The specification asserts that the invention provides “means for the production of lipid compositions exhibiting such strong difference in contents between EPA and ARA.” *Id.* at 3:25-28. It further asserts that it was “surprising that such a marked difference could be maintained in plant lipid compositions [] because both ARA and EPA are produced by the same class of enzymes, that is Delta-5 desaturases, and typically a Delta-5 desaturase producing EPA will also produce ARA.” *Id.* at 3:28-34. The specification further asserts—falsely—that “ARA and EPA are converted *into each other* by action of omega 3 desaturases naturally present in material or introduced into the plant”⁴ (emphasis added) and that it was “therefore expected that the composition of plant lipids could not be tilted in favour of high EPA contents without also increasing ARA content.” *Id.* at 3:34-40. Ex. 1002, ¶46.

⁴ As explained in section IV.B.2, omega-3 desaturases can convert ω 6-fatty acids such as ARA to EPA but cannot convert EPA (an ω 3-fatty acid) to ARA.

a. The Delta-5 elongase expression disclosure

To achieve the claimed lipid profile, the specification asserts that “[t]he inventors have found that by carefully regulating the expression particularly of Delta-5 elongase activity it is possible to achieve the desired reduction in ARA lipids while maintaining ongoing synthesis of EPA and/or DHA.” Ex. 1001, 7:26-30. In particular, the specification states that a plant or plant material of the invention preferably comprises “a Delta-5 elongase gene under the control of a promoter such that expression of the Delta-5 elongase gene is maintained or increased in late stage seed development.” *Id.* at 7:19-23. Ex. 1002, ¶47.

To maintain or increase expression of the Delta-5 elongase in late stage seed development, the specification asserts as follows:

Gene expression can be regulated by any means available to the skilled person. For example, gene expression can be achieved by creating the appropriate construct topology such that transformed nucleic acids [] will, by their very own arrangement of promoters, genes and terminators [] achieve the desired regulation pattern. For example, an expression cassette comprising a promoter and operably linked thereto a Delta-5 elongase gene located in the vicinity of another promoter exhibiting strong late stage seed development gene expression can allow for maintained or increased expression of the Delta-5 elongase gene in late stage seed development.

[...]

Increased Delta-5 elongase gene expression can also be achieved by the action of an inductor, such that at least one Delta-5 elongase gene is under the control of an inducible promoter; increase can also be achieved by removal of a repressor, such that the repressor is only being produced during early stages of seed development.

Ex. 1001 at 7:32-65. Ex. 1002, ¶48.

Each of these assertions appears to be entirely hypothetical and unsupported by data. Despite asserting how to achieve the desired expression profile, the specification ***does not contain*** any description of (1) the “appropriate construct topology” to achieve the claimed expression pattern (2) promoters that should be used to control expression of the Delta-5 elongase, (3) other promoters the Delta-5 elongase gene should be located “in the vicinity of,” (4) what type of inducible promoter should be used, or (5) what type or repressor should be used. Ex. 1002, ¶49.

Notably, in the ***entire*** discussion of how to achieve the desired expression profile for a Delta-5 elongase, the specification ***does not*** contain any assertion or claim that putting a Delta-5 elongase under the control of a “FAE promoter” achieves the desired expression profile. Indeed, there is no disclosure in the ‘095 Patent whatsoever of a “FAE” promoter, let alone a “Delta-5 elongase under the control of a FAE promoter.” Ex. 1002, ¶50.

b. Example 1 of the '095 Patent

The specification of the '095 contains five Examples which focus on analysis of lipids extracted from homozygous T3 or T4 plants of transgenic events denoted "LBFLFK," "LBFGKN," "LANPMZ," and "LAODDN." Ex. 1002, ¶51.

Example 1 explains that T3 or T4 plants of events "LBFLFK," "LBFGKN," "LANPMZ," and "LAODDN" were grown and seeds collected at various time points for lipid extraction and analysis. Example 1 provides the *names* of the genetic constructs used for each of these transgenic events but ***does not*** describe the full contents of each genetic construct. Example 1 only explains that all events comprise "one gene coding for a Delta-5 elongase based on that obtained from *Ostreococcus tauri*," and "one gene coding for a Delta-5 desaturase based on that obtained from *Thraustochytrium* sp." and "[e]vents LBFLFK and LBFGKN contain a further copy of the Delta-5 desaturase gene under the control of another promoter (SETL instead of Conlinen)". The specification of the '095 Patent ***does not*** provide any further description of the contents of each event or genetic construct. In particular, the specification of the '095 Patent ***does not*** describe the full contents of the constructs used to generate plants of events "LBFLFK," "LBFGKN," "LANPMZ," and

“LAODDN” and *does not* describe what promoter controls expression of the Delta-5 elongase in these transgenic events.⁵ Ex. 1002, ¶52.

c. Example 2 of the ‘095 Patent

Example 2 simply outlines the techniques used to extract and analyze the fatty acid of lipids extracted from seeds collected in Example 1. *See* Ex. 1001, 10:19-11:23. Ex. 1002, ¶53.

d. Example 3 of the ‘095 Patent

Example 3 describes the quantitative real-time PCR (qPCR) protocol used to measure the mRNA concentrations of various transgenes in seeds for each transgenic event at various times after flowering. *See* Ex. 1001, 11:25-12:45. Ex. 1002, ¶ Ex. 1002, ¶54.

e. Example 4 of the ‘095 Patent

Example 4 describes the analysis of mRNA concentrations determined using the protocols outlined in Example 3, providing two tables (“QPCR1” and “QPCR2”) showing total Delta-5 elongase and Delta-5 desaturase mRNA quantity,

⁵ As explained in section V.B.1, the provisional applications show that the genetic constructs used to produce events “LBFLFK,” “LBFGKN,” “LANPMZ,” and “LAODDN” all used *the same Brassica napus* FAE1.1 promoter to control expression of the Delta-5 elongase.

respectively. Ex. 1001, 15:33-16:28. Example 4 explains that expression of the Delta-5 elongase gene of the events LBFGKN and LBFLFK “continued even after 30 days after flowering, whereas expression the Delta-5 elongase gene of the events LANPMZ and LAODDN was severely reduced or only marginally detectable after 30 days of flowering.” Ex. 1001, 15:25-30. Ex. 1002, ¶55.

f. Example 5 of the ‘095 Patent

Example 5 of the ‘095 Patent provides the fatty acid composition of seed lipids of the events analyzed using the techniques outlined in Example 2. It explains that “the content of ARA in total extracted seed lipids of events LANPMZ and LAODDN did not significantly decrease over time, whereas the content of ARA [] in total extracted seed lipids of events LBFGKN and LBFLFK decreased by 0.53% and 0.72%, respectively” Ex. 1001, 16:31-38. It also explains that “only for events LBFGKN and LBFLFK a difference in EPA and ARA content of more than 5% could be achieved and a difference in (EPA+DHA) and ARA content of more than 7% could be achieved.” Ex. 1001, 16:45-49. Ex. 1002, ¶56.

B. The disclosure of the provisional applications

The ‘622 and ‘373 applications are nearly identical, with identical Figures and a nearly identical specification. The ‘373 application contains everything in the ‘622 application except for minor changes to the detailed description and an additional four examples. Each provisional application relates, generally, to plants transformed

with genetic constructs containing enzymes in the aerobic biosynthetic pathway of long-chain polyunsaturated fatty acids (“LC-PUFAs”) summarized in section IV.B, *supra*. Ex. 1002, ¶57.

Examples 1-28 of the ‘622 and ‘373 applications appear to be essentially identical, with only minor formatting differences found between these examples in the two priority documents. Examples 1-20 of the provisional applications relate to the assembly of genetic constructs containing enzymes in the aerobic biosynthetic pathway of long-chain polyunsaturated fatty acids and the transformation and analysis of plants transformed with these constructs. Examples 21-28 further describe experiments and analysis of various elements of the genetic constructs and the fatty acids produced by plants transformed with the genetic constructs. Ex. 1002, ¶58.

The ‘373 application contains additional Examples 29-32. Examples 29-32 of the ‘373 application relate to the analysis of oils from commercial oil samples and oils produced in transgenic plants transformed with the genetic constructs described in the provisional applications. Ex. 1002, ¶59.

1. The genetic constructs in events “LBFLFK,” “LBFGKN,” “LANPMZ,” and “LAODDN”

As discussed above, the specification of the ‘095 Patent **does not describe** the full contents of any of the genetic constructs used to generate the events “LBFLFK,”

“LBFGKN,” “LANPMZ,” and “LAODDN” analyzed in the Patent. Instead the ‘095 Patent merely explains that (1) the “LBFLFK” event contains “two copies of VC-LTM593-1qcz rc”; (2) the “LBFGKN” event contains “one copy of VC-LTM593-1qcz rc”; (3) the “LANPMZ” event contains “one copy of each of VC-LJB2197-1qcz and VC-LLM337-1qcz rc”; and the “LAODDN” event contains “one copy each of VC-LJB2755-2qcz rc and VC-LLM391-2qcz rc.” The contents of these genetic constructs are **not described anywhere** in the ‘095 Patent but do appear to be described in the provisional applications. Table 13 of the ‘622 application—reproduced and annotated below—summarizes the genes and promoters present in the various combinations of genetic constructs exemplified in the provisional applications. It shows that each of the events “LBFLFK,” “LBFGKN,” “LANPMZ,” and “LAODDN” all contained a Delta-5 elongase under the control of a *Brassica napus* FAE1.1 promoter.⁶ Ex. 1002, ¶60.

⁶ The second column of Table 13 summarizes the contents of the genetic constructs contained in event “LANPMZ,” the fourth column summarizes the contents of the genetic constructs contained in event “LAODDN,” and the last column summarizes the contents of the genetic construct contained in events “LBFLFK,” and “LBFGKN.” Tables 4, 6, and 11 show that “BnFae1” refers to the “[p]romoter from

Beta-*KETOACYL-CoA SYNTHASE (FAE1.1)* gene from *Brassica napus*.” See
Ex. 1005, pp. 419, 422, and 440.

Table 13: Order and orientation of plant expression cassettes on T-DNAs. Per column, expression cassettes are abbreviated according to Table 12 and listed from top to bottom in the following way: The top row indicated the right border of the first T-DNA introduced into the plant genome; the following proteins are all listed according to sense orientation of transcription, pointing away from the right border. The end of the first T-DNA was indicated by 'LB'. In case a second T-DNA was used to transfer all pathway genes into the plant genome according to example 7 to 11, the right border of this T-DNA was indicated as 'RB2'. The expression cassettes of the second T-DNA are listed in the following rows. Empty cells have been introduced to facilitate comparison of the different constructs.

VC-LJB2197-1qcz + VC-LLM306-1qcz rc	VC-LJB2197-1qcz + VC-LLM337-1qcz rc	VC-LJB2197-1qcz + VC-LLM338-3qcz rc	VC-LJB2755-2qcz + VC-LLM391-2qcz rc	VC-LJB2755-2qcz + VC-LLM217-1qcz rc	RTP10690-1qcz_F	RTP10691-2qcz	VC-LMT595-1qcz rc	VC-LMT593-1qcz rc
RB	RB	RB	RB	RB	RB	RB	RB	RB
USP/c- d6Elo(Pp_GA2)	USP/c- d6Elo(Pp_GA2)	USP/c- d6Elo(Pp_GA2)	PXR/c- o3Des(Pir_GA)	PXR/c- o3Des(Pir_GA)	USP/c- d6Elo(Pp_GA2)	USP/c- d6Elo(Pp_GA2)	USP/c- d6Elo(Pp_GA2)	USP/c- d6Elo(Pp_GA2)
Conlinin/c- d5Des(Tc_GA2)	Conlinin/c- d5Des(Tc_GA2)	Conlinin/c- d5Des(Tc_GA2)	Conlinin/c- d5Des(Tc_GA2)	Conlinin/c- d5Des(Tc_GA2)	Conlinin/c- d5Des(Tc_GA2)	Conlinin/c- d5Des(Tc_GA2)	Conlinin/c- d5Des(Tc_GA2)	Conlinin/c- d5Des(Tc_GA2)
SBP/c- d6Des(Ot_febit)	SBP/c- d6Des(Ot_febit)	SBP/c- d6Des(Ot_febit)	SBP/c- d6Des(Ot_febit)	SBP/c- d6Des(Ot_febit)	SBP/c- d6Des(Ot_febit)	SBP/c- d6Des(Ot_febit)	SBP/c- d6Des(Ot_febit)	SBP/c- d6Des(Ot_febit)
PXR/c- d6Elo(Tp_GA2)	PXR/c- d6Elo(Tp_GA2)	PXR/c- d6Elo(Tp_GA2)	FAE/c- d6Elo(Tp_GA2)	FAE/c- d6Elo(Tp_GA2)	PXR/c- d6Elo(Tp_GA2)	PXR/c- d6Elo(Tp_GA2)	PXR/c- d6Elo(Tp_GA2)	PXR/c- d6Elo(Tp_GA2)
Napin/c- d12Des(Ps_GA)	Napin/c- d12Des(Ps_GA)	Napin/c- d12Des(Ps_GA)	Napin/c- d12Des(Ps_GA)	Napin/c- d12Des(Ps_GA)	Napin/c- d12Des(Ps_GA)	Napin/c- d12Des(Ps_GA)	Napin/c- d12Des(Ps_GA)	Napin/c- d12Des(Ps_GA)
			USP/c- o3Des(Pi_GA2)	USP/c- o3Des(Pi_GA2)	PXR/c- o3Des(Pir_GA)	PXR/c- o3Des(Pir_GA)	PXR/c- o3Des(Pir_GA)	
UBI/AHAS	UBI/AHAS	UBI/AHAS	UBI/AHAS	UBI/AHAS				
LB	LB	LB	LB	LB				
RB2	RB2	RB2	RB2	RB2				
Conlinin/d4Des(Eg)	Conlinin/d4Des(Eg)				Conlinin/c- d4Des(Pi_GA)2_var 1	SETL/c- d5Des(Tc_GA2)	SETL/c- d5Des(Tc_GA2)	SETL/c- o3Des(Pir_GA)
FAE/c- d5Elo(Ot_GA3)	FAE/c- d5Elo(Ot_GA3)	FAE/c- d5Elo(Ot_GA3)	FAE/c- d5Elo(Ot_GA3)	FAE/c- d5Elo(Ot_GA3)	FAE/c- d5Elo(Ot_GA3)	FAE/c- d5Elo(Ot_GA3)	FAE/c- d5Elo(Ot_GA3)	USP/c- o3Des(Pi_GA2)
SETL/c- o3Des(Pir_GA)	SETL/c- o3Des(Pir_GA)							SETL/c- d5Des(Tc_GA2)
					ARC/c- d4Des(Tc_GA) var2	ARC/c- d4Des(Tc_GA) var2	ARC/c- d4Des(Tc_GA) var2	ARC/c- d4Des(Tc_GA) var2
USP/c- o3Des(Pi_GA2)	USP/c- o3Des(Pi_GA2)	USP/c- o3Des(Pi_GA2)			USP/c- o3Des(Pi_GA2)	USP/c- o3Des(Pi_GA2)	USP/c- o3Des(Pi_GA2)	PXR/c- o3Des(Pir_GA)
ARC/c- d4Des(Tc_GA) var 1	ARC/c- d4Des(Tc_GA) var 1	ARC/c- d4Des(Tc_GA) var 1	ARC/c- d4Des(Tc_GA) var 1	ARC/c- d4Des(Tc_GA) var 1	SETL/c- d5Des(Tc_GA2)			Conlinin/c- d4Des(Pi_GA)2_var 1
		Conlinin/d4Des(Eg)	Conlinin/d4Des(Eg)	Conlinin/c- d4Des(Pi_GA)2_var 2		FAE/c- d4Des(Pi_GA)2	FAE/c- d4Des(Pi_GA)2	FAE/c- d5Elo(Ot_GA3)
					SETL/c- o3Des(Pir_GA)	SETL/c- o3Des(Pir_GA)	SETL/c- o3Des(Pir_GA)	
					UBI/AHAS	UBI/AHAS	UBI/AHAS	UBI/AHAS

Ex. 1005, p. 445; Ex. 1002, ¶60.

2. The generic concept of using a “Delta-5 elongase under the control of a FAE promoter” is not found anywhere in the priority applications

Although the provisional applications describe specific genetic constructs containing a Delta-5 elongase from *Ostreococcus tauri* under the control of a *Brassica napus* FAE1.1 promoter, they do not recite—*anywhere*—the generic concept of a “Delta-5 elongase under the control of a FAE promoter.” Indeed “FAE promoter” as a generic concept is not found *at all* the in the provisional applications. The sole reference in the provisional applications to any “FAE” promoter is in tables and figures of the provisional applications which describe genetic constructs that contain a specific *Brassica napus* FAE1.1 promoter. In *all* cases, these tables and figures specifically recite either “bnFae1,” or “Promoter from *Beta-KETOACYL-CoA SYNTHASE (FAE1.1)* gene from *Brassica napus*.” Ex. 1002, ¶61.

3. The priority applications do not describe the concept of a *Brassica napus* plant with the levels of ARA, EPA, and DHA recited in the claims

The claims of the ‘095 Patent recite *Brassica napus* plants or parts thereof where the lipids found in the seeds (1) have a content of EPA that is at least 5% higher than that of ARA, (2) have a sum of EPA+DHA content that is at least 7% higher than ARA, and/or (3) the content of ARA is less than 4%, the content of EPA is more than 7%, and the content of DHA is more than 2%. Ex. 1002, ¶62.

The provisional applications do not describe *Brassica napus* plants with these levels or ARA, EPA, and DHA. Ex. 1002, ¶63.

Further, claims 3 and 4 recite harvesting *Brassica napus* plants when the contents of ARA has decreased and claims 9-11 recite plants wherein, when grown, the content of ARA decreases or the content of EPA and/or DHA increase. Ex. 1002, ¶64.

Again, the provisional applications do not describe harvesting *Brassica napus* plants when the content of ARA has decreased and do not describe the content of ARA decreasing or the content of EPA increasing in *Brassica napus* plants when grown. Ex. 1002, ¶65.

4. The priority applications do not describe the concept of a *Brassica napus* plant where the recited levels of EPA, ARA, and DHA are a result of the $\Delta 5$ -elongase being under the control of a FAE promoter

As discussed in section V.A.2, the specification recites the concept of a “Delta-5 elongase under the control of a promoter such that expression of the Delta-5 elongase is maintained or increase in late stage seed development.” The claims recite, *inter alia*, levels of EPA and/or DHA that are higher than the level of ARA, with the specification asserting that “by carefully regulating the expression particularly of Delta-5 elongase activity it is possible to achieve the desired reduction

in ARA lipids while maintaining ongoing synthesis of EPA and/or DHA.” Ex. 1001, 7:26-30. Ex. 1002, ¶66.

However, the provisional applications do not contain *any* assertion that “carefully regulating the expression particularly of Delta-5 elongase activity” will lead to the recited levels of EPA, DHA and ARA. Moreover, there is no assertion in the provisional applications that putting a Delta-5 elongase under the control of a FAE promoter (as recited in the claims) achieves the levels of EPA, DHA and ARA recited in the claims. Ex. 1002, ¶67.

C. Examination of the ‘162 application

1. Summary of the prosecution history of the ‘162 application

a. Initial filing

The ‘162 application was initially filed with claim 1 directed to:

Extracted *Brassica napus* plant lipid composition comprising eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) and optionally arachidonic acid (ARA), wherein

- a) the content of EPA is at least 5% higher than of ARA, and/or
- b) the sum of contents of EPA+DHA is at least 7% higher than ARA, and/or
- c) the content of ARA is less than 4% and the content of EPA is more than 7% and the content of DHA is more than 2%.

Ex. 1007, p. 62. Ex. 1002, ¶68.

Claim 2 recited a *Brassica napus* plant or part thereof, comprising lipids with the same features recited in claim 1. Claim 5 depended from claim 5 and further specified that the *Brassica napus* plant comprises:

- a) a Delta-5 elongase gene under the control of a promoter such that expression of the Delta-5 elongase gene is maintained or increased in late stage seed development, and/or
- b) a Delta-5 desaturase gene under the control of a promoter such that expression of the Delta-5 desaturase gene is reduced or prevented in late stage seed development.

Ex. 1007, p. 62. Ex. 1002, ¶69.

b. March 5, 2020 Office Action

In the first Office Action on the merits, issued on March 5, 2020, claims 10-12 were withdrawn from consideration as directed to a non-elected invention and rejected then-pending claims 1-9 and 13-18 under 35 U.S.C. § 103 as obvious over PCT International Patent Application Publication No. WO 2013/153404 (“the ‘404 publication”, Ex. 1008.) Ex. 1007, pp. 929-931.⁷ Ex. 1002, ¶70.

⁷ The Examiner also rejected then-pending claims 1-4, 6-9 and 13-18 under 35 U.S.C. § 101 as directed to a product that does not markedly differ from its closest naturally-occurring counterpart. Ex. 1007, pp. 922-929.

c. September 4, 2020 Amendment

In response to the March 5, 2020 Office Action, in a September 4, 2020 Amendment, Patent Owner (“PO”) cancelled claim 1 and amended claim 2 to recite “wherein the *Brassica napus* plant or part thereof comprises a Delta-5 elongase gene under the control of a promoter such that expression of the Delta-5 elongase gene is maintained or increased in late stage seed development.” PO also amended claim 3 to recite that “the content of EPA and/or DHA in the lipids of the seeds increases during late stage seed development” and amended claim 4 to recite that the content of “EPA in the lipids of the seeds increases at least 1.0% by weight of total lipids during late stage seed development.” Further, PO amended claim 7 to recite, *inter alia*, a step of “harvesting seeds of the plant when, after the peak of ARA content, the ARA content has decreased and the EPA and/or DHA content in the lipids has increased in the lipids of the developing seeds...” Ex. 1007, pp. 971-972. Ex. 1002, ¶71.

Regarding the rejection of claim 2 under 35 U.S.C. § 103, PO argued that “WO 2013/153404 provides no teaching or suggestion to provide a *Brassica napus* plant with a Delta-5 elongase gene under the control of a promoter such that expression of the Delta-5 elongase gene is maintained or increased in late stage seed development.” PO argued that Figure 2 of WO 2013/153404 shows that the delta-5 elongase “was driven by the conlinen1 promoter,” citing to Truksa et al., Plant

Physiology and Biochemistry 41 (2003) 141-147 (“Truksa”, Ex. 1009) to allege that such conlinen1 promoter has “very little activity in 40-day old seeds”. Ex. 1007, p. 976. Regarding claim 7, PO similarly asserted that “Figure 2 of WO 2013/153404 shows that the delta-5 elongase in WO 2013/153404 was driven by the conlinen1 promoter” and that “[t]here is simply no teaching, suggestion, or motivation that would have led a person of skill in the art to modify the conlinen1 promoter to achieve the recited increase in EPA and/or DHA and decrease in ARA during late stage seed development...” Ex. 1007, p. 977. Ex. 1002, ¶72.

d. December 8, 2020 Final Office Action

In response to PO’s September 4, 2020 Amendment, the Examiner issued a December 8, 2020 Final Office Action which maintained the rejection of claims 1-9 and 13-18 under 35 U.S.C. § 103 for the reasons provided in the March 5, 2020 Office Action. In response to PO’s arguments, the Examiner asserted that the claims “do not recite a particular promoter” and the ‘404 publication “also discloses the use of other promoters.” Ex. 1007, p. 994. The Examiner further dismissed PO’s citation to Truksa, asserting that “this reference teaches protein conlinin as a seed specific promoter for flax seed protein” which is “in stark contrast from promoting Delta 5 elongase gene expression of EPA + DPA.” Ex. 1007, pp. 994-995. Ex. 1002, ¶73.

e. May 10, 2021 Amendment

In response to the December 8, 2020 Final Office Action, in a May 10, 2021 Amendment, PO amended all pending independent claims to recite a “a Delta-5 elongase gene under the control of a FAE promoter.” Ex. 1007, pp. 1015-1016. PO asserted that support for this amendment to recite a FAE promoter “is found throughout U.S. Provisional Patent Applications 62/079,622 and 62/234,373, which were incorporated by reference in the current application (see, e.g., Application No. 62/079,622 at pages 62, 63,67, 75, 76, 80 and Application No. 62/234,373 at page 68.)” In response to the outstanding rejection under 35 U.S.C. § 103, PO asserted that “[t]he cited prior art does not teach or suggest using a FAE promoter, let alone using such a promoter in a Brassica napus plant to drive expression of a Delta-5 elongase gene” and that there is “no teaching or suggestion that using a FAE promoter to drive expression of a Delta-5 elongase gene is a Brassica napus plant would result in the claimed lipid profile, which was surprising.” Ex. 1007, p. 1018 (emphasis in original). Ex. 1002, ¶74.

f. June 3, 2021 Office Action and allowance

Following PO’s May 10, 2021 Amendment, the Examiner issued a June 3, 2021 Office Action in which all outstanding rejections to claims 2-4, 6 and 16-20 were withdrawn. The Examiner also presented a new rejection of claims 7 and 13-

15 under 35 U.S.C. §103.⁸ Ex. 1007, p. 1024-1027. Following PO's cancellation of claims 7 and 13-15, claims 10-12 were rejoined and claims 2-4, 6, 10-12, and 16-20 were allowed on October 20, 2021. Ex. 1007, pp. 1038-1042 and 1055. Ex. 1002, ¶75.

At no point during prosecution of the '162 application did the Examiner raise a rejection of the claims under 35 U.S.C. § 112 for lack of enablement or written description. Similarly, there is no record of the Examiner properly considering the anticipatory prior art references raised in this petition. Ex. 1002, ¶76.

D. The data in the '095 Patent show that “Delta-5 elongase under the control of a FAE promoter” is not responsible for the recited levels of EPA, DHA and ARA

1. The same *Brassica napus* FAE1.1 promoter was present in all transgenic *Brassica napus* plants exemplified in the '095 Patent

As discussed in section V.B.1, *all* of the events “LBFLFK,” “LBFGKN,” “LANPMZ,” and “LAODDN” described in the '095 Patent contained a Delta-5 elongase under the control of a *Brassica napus* FAE1.1 promoter. Ex. 1002, ¶77.

⁸ Because these claims were ultimately cancelled by PO, this rejection is not being addressed in this petition.

2. *Brassica napus* plants expressing a $\Delta 5$ -elongases under the control of a *Brassica napus* FAE1.1 promoter did not achieve the levels of EPA, DHA and ARA recited in the claims

Example 4 of the '095 Patent explains that expression of the Delta-5 elongase gene of the events LBFGKN and LBFLFK “continued even after 30 days after flowering, whereas expression the Delta-5 elongase gene of the events LANPMZ and LAODDN was severely reduced or only marginally detectable after 30 days of flowering.” However, all transgenic events contained a Delta-5 elongase under the control of a *Brassica napus* FAE1.1 promoter (*see* section V.B.1). Therefore, it would be clear to a POSITA that the maintenance or increase in Delta-5 elongase expression in late stage seed development observed for events LBFGKN and LBFLFK was not caused by the use of a *Brassica napus* FAE1.1 promoter to control expression of the $\Delta 5$ -elongase. Ex. 1002, ¶78.

Further, despite all transgenic events containing a Delta-5 elongase under the control of a *Brassica napus* FAE1.1 promoter (*see* section V.B.1), only events “LBFLFK” and “LBFGKN” produced seed comprising lipids with levels of EPA, DHA and ARA (barely) within the scope of the recited claims, while seeds from events “LANPMZ” and “LAODDN” comprised levels of EPA, DHA and ARA falling outside of the scope of the claims. Based on this data, it would be clear to a POSITA that the recited levels of EPA, DHA, and ARA are not attributable to the

use of a *Brassica napus* FAE1.1 promoter to control expression of the $\Delta 5$ -elongase.

Ex. 1002, ¶79.

3. Publications in the art demonstrate that the use of a *Brassica napus* FAE1.1 promoter is likely not responsible for expression of the $\Delta 5$ -elongase during late stage seed development

In addition to the evidence in the ‘095 Patent itself, a review of the literature demonstrates that the genus of “FAE” promoters do not necessarily cause a maintenance or increase of gene expression during late stage seed development. Rossak, et al. (2001). *Plant Molecular Biology*, 46(6), 717-725 (“Rossak”, Ex. 1015) is a prior art publication which describes the temporal and spatial expression of the *Arabidopsis* FAE1 gene. Rossak demonstrates that the FAE1 promoter from *Arabidopsis* causes gene expression to increase rapidly to around 11 days after flowering (DAF), followed by a *gradual decline in maturing seeds*. Ex. 1015, p. 8, left-hand column, second full paragraph. Ex. 1002, ¶80.

While the ‘095 application asserts that the claimed levels of ARA, EPA, and DHA are achieved by maintenance or increase in Delta-5 elongase expression in late stage seed development, the claims require the presence of a Delta-5 elongase under the control of an FAE promoter. As discussed above, neither the *Brassica napus* FAE1.1 promoter exemplified in the ‘095 patent nor the *Arabidopsis* FAE1 promoter

cause the expression of the Delta-5 elongase to be maintained or increased in late stage seed development. Ex. 1002, ¶81.

VI. STATEMENT OF THE PRECISE RELIEF REQUESTED AND THE REASONS THEREFOR UNDER 37 C.F.R. § 42.22(A) AND 37 C.F.R. § 42.204(B)

CSIRO respectfully requests post-grant review, and cancellation, of claims 1-11 of the '095 Patent under 35 U.S.C. § 321 based on the following unpatentability grounds:

<u>Ground</u>	<u>Statute</u>	<u>Challenge</u>	<u>Claims</u>
1	§112(a)	Lack of written description for a <i>Brassica napus</i> plant or part thereof comprising “a Delta-5 elongase gene under the control of a FAE promoter”	1-11
2	§112(a)	Lack of written description for a <i>Brassica napus</i> plant or part thereof comprising lipids wherein “the content of EPA is at least 5% higher than of ARA”	1-8
3	§112(a)	Lack of written description for a <i>Brassica napus</i> plant or part thereof comprising lipids wherein “the sum of contents of EPA+DHA is at least 7% higher than ARA”	1-8
4	§112(a)	Lack of written description for a <i>Brassica napus</i> plant or part thereof comprising lipids wherein “the content of ARA is less than 4% and the content of EPA is more than 7% and the content of DHA is more than 2%”	1-8

<u>Ground</u>	<u>Statute</u>	<u>Challenge</u>	<u>Claims</u>
5	§112(a)	Lack of written description for a <i>Brassica napus</i> plant “wherein the content of EPA in the lipids of the seeds increases at least 1.0% by weight of total lipids during late stage seed development”	10
6	§112(a)	Lack of written description for the full scope of “harvesting the plants or a part thereof when the lipids content of ARA in the lipids of the seeds has decreased”	3-4
7	§112(a)	Lack of enablement of a <i>Brassica napus</i> plant or part thereof comprising lipids wherein “the content of EPA is at least 5% higher than of ARA”	1-8
8	§112(a)	Lack of enablement of a <i>Brassica napus</i> plant or part thereof comprising lipids wherein “the sum of contents of EPA+DHA is at least 7% higher than ARA”	1-8
9	§112(a)	Lack of enablement of a <i>Brassica napus</i> plant or part thereof comprising lipids wherein “the content of ARA is less than 4% and the content of EPA is more than 7% and the content of DHA is more than 2%”	1-8
10	§112(a)	Lack of enablement of a <i>Brassica napus</i> plant wherein, when the <i>Brassica napus</i> plant or part thereof is grown, the content of ARA in the lipids of the seeds decreases at least 0.5% by weight of total lipids and the content of EPA and/or DHA in the lipids of the seeds increases	9-11

<u>Ground</u>	<u>Statute</u>	<u>Challenge</u>	<u>Claims</u>
11	§112(a)	Lack of enablement of a <i>Brassica napus</i> plant “wherein the content of EPA in the lipids of the seeds increases at least 1.0% by weight of total lipids during late stage seed development”	10
12	§112(a)	Lack of enablement of the full scope of “harvesting the plants or a part thereof when the lipids content of ARA in the lipids of the seeds has decreased”	3-4
13	§102(a)	Anticipation by PCT International Application Publication No. WO 2013/185184	1 and 6
14	§102(a)	Anticipation by PCT International Application Publication No. WO 2015/089587	1 and 6

A. Claim construction (37 C.F.R. § 42.204(b)(3))

Claims in PGR petitions filed after November 13, 2018, are construed using the same standard as in district court. *See* 83 Fed. Reg. 51340 (Oct. 11, 2018); *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (*en banc*). Specifically, claims are construed in accordance with the ordinary and customary meaning of such claims as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent. 37 C.F.R. § 42.200(b). Claim terms are generally given their “ordinary and customary meaning,” that is, “the meaning that the term would have to a POSITA in question at the time of the invention, i.e., as the effective filing date of the patent application.” *Id.* at 1313. For this Petition,

Petitioner submits that claim terms not included in the following discussion should be given their ordinary and customary meaning.

1. EPA, DHA, and ARA

Claim 1 recites a plant that produces eicosapentaenoic acid (EPA) and/or docosapentaenoic acid (DHA) and optionally Arachidonic Acid (ARA). Such terms should be given their ordinary and customary meaning to a POSITA. Given their ordinary and customary meaning, EPA, DHA, and ARA are as discussed in section IV.A, *supra*. Ex. 1002, ¶82.

Claim 1 also recites *Brassica napus* plant or part thereof, comprising seeds that comprise lipids wherein “a) the content of EPA is at least 5% higher than of ARA, and/or b) the sum of contents of EPA+DHA is at least 7% higher than ARA and/or c) the content of ARA is less than 4% and the content of EPA is more than 7% and the content of DHA is more than 2%.” Column 4, lines 32-35 of the ‘095 Patent explains that “lipids content is expressed as weight percentage of a specific fatty acid relative to total fatty acids determined in the respective lipids composition.” Thus, where the content of EPA is at least 5% higher than of ARA as recited in claim 1 subpart a), the claim encompasses *Brassica napus* seeds comprising a 5-100% EPA. Where the sum of contents of EPA+DHA is at least 7% higher than ARA as recited in claim 1 subpart b), the claim encompasses *Brassica*

napus seeds comprising 7-100% EPA+DHA.⁹ Where the content of ARA is less than 4% and the content of EPA is more than 7% and the content of DHA is more than 2% as recited in claim 1 subpart c), the claim encompasses *Brassica napus* seeds comprising a 7-98% EPA, 2-93% DHA, and 0-4% ARA. Ex. 1002, ¶83.

2. Delta-5 elongase

Each of the claims of the '095 Patent recite a "Delta-5 elongase gene under the control of a FAE promoter." Given its ordinary and customary meaning, a "Delta-5 elongase gene" refers to a gene that encodes a Δ 5-elongase, i.e. a gene that encodes an enzyme that inserts a two-carbon unit at the carboxyl end of fatty acid chains having their first double-bond at the Δ 5 position as discussed in section IV.B.1, *supra*. Ex. 1002, ¶84.

3. FAE promoter

The "FAE promoter" is not recited or defined anywhere in the '095 Patent. Nevertheless, given its ordinary customary meaning, a "FAE promoter" refers to a promoter that is naturally associated with a "Fatty Acid Elongation" or "Fatty Acid Elongase" gene of an organism. As discussed in section IV.B.3, Promoters of FAE genes have been identified in various species, including *Arabidopsis thaliana*,

⁹ This amount would including a DHA content of 100% and an EPA content of 0%, or vice versa.

Brassica napus, *Brassica rapa*, *Brassica nigra*, *Brassica juncea*, and *S. chinensis*.

Ex. 1002, ¶85.

4. Late-stage seed development

Claims 8, 10 and 11 refer to “late-stage seed development.” This term is not defined anywhere in the ‘095 Patent. However, based on the discussion at column 9, lines 45-63, and in Example 4 of the ‘095 patent, “late-stage seed development” may refer to approximately 30 days after flowering for *Brassica napus* plants. Ex. 1002, ¶86.

B. Person of ordinary skill in the art

A person of ordinary skill in the art (a “POSITA”) as of the date of invention would have had at least a Ph.D. in molecular biology, molecular genetics, biochemistry, or a related field and at least 3-5 years of research work experience (excluding Ph.D. thesis studies) in molecular genetics or biology, plant genetics, recombinant DNA techniques, seed developmental biology, plant physiology, or lipid metabolism. An individual need not have every qualification enumerated above and more experience, such as research work in a closely related field, can compensate for less formal education. Ex. 1002, ¶16.

VII. THE ‘095 PATENT IS PGR ELIGIBLE

The PGR provisions of the Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) (“AIA”) apply to patents “described in section

3(n)(1)” of the AIA, i.e. any patent issuing from an application that **contains, or contained at any time**, (A) a claim to a claimed invention that has an “effective filing date” that is on or after March 16, 2013, or (B) “a specific reference under section 120, 121, or 365(c) of title 35, United States Code, to any patent or application that contains or contained at any time such a claim”. *See* AIA, § 3(n)(1).

U.S. Provisional Application No. 62/079,622—the earliest application to which it claims priority—was filed on November 14, 2014. Accordingly, the PGR provisions of the AIA apply to the subject application. *See* AIA, § 3(n)(1).

VIII. CLAIMS 1-11 OF THE ‘095 PATENT ARE UNPATENTABLE

A. The claims lack entitlement to priority

As discussed in section V.B, the provisional applications do not describe many of the features recited in claims 1-11, including (1) the recited levels of ARA, EPA, and DHA, (2) harvesting plants when the level of ARA has decreased, or (3) plants wherein, when grown, the content of ARA decreases or the content of EPA and/or DHA increases. Accordingly, claims 1-11 are not entitled to priority of either of the provisional applications. Ex. 1002, ¶87.

B. Grounds 1-6: The claims lack written description support

1. Legal standard for written description

Section 112(a) contains a written description requirement separate from the enablement requirement. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1344 (Fed. Cir. 2010) (en banc). To satisfy the written description requirement, an application must “reasonably convey [] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.” *Ariad v. Lilly* at 1351. This requirement is not satisfied by an earlier disclosure that merely renders the later claimed invention obvious; rather, the earlier filed application must describe the claimed invention with all its limitations. *See Tronzo v. Biomet, Inc.*, 156 F.3d 1154, 1158 (Fed. Cir. 1998).

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. *See Regents of the Univ. of Cal. v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Satisfactory disclosure of a “representative number” depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, disclosure of a single species within a genus which embraces widely variant species has been found to be insufficient to support written description of the genus. *See, e.g., Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Instead, the disclosure must adequately reflect the structural diversity of the claimed genus, either through the disclosure of sufficient species that are “representative of the full variety or scope of the genus,” or by the establishment of “a reasonable structure-function correlation.” Such correlations may be established “by the inventor as described in the specification,”

or they may be “known in the art at the time of the filing date.” *See AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1300-01, 111 USPQ2d 1780, 1790-91 (Fed. Cir. 2014). See also *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989) (generic and subgeneric claims in the U.S. application were not entitled to the benefit of foreign priority where the foreign application disclosed only two of the species encompassed by the broad generic claim and the subgeneric Markush claim that encompassed 21 compounds).

Under 37 CFR 1.57(d), essential material “may be incorporated by reference, but only by way of an incorporation by reference to a U.S. patent or U.S. patent application publication. “Essential material” is material that is necessary to, *inter alia*, “[p]rovide a written description of the claimed invention.” 37 CFR 1.57(d). Further, a provisional application is not a “U.S. patent application publication” under this rule. *ZTE (USA), Inc. and LG Electronics Inc., v. Cywee Group Ltd.*, IPR2019-00143, Paper 87, p. 115 (PTAB Feb. 17, 2021) citing *Nomadix, Inc. v. Second Rule LLC*, No. CV0701946DDPVBKX, 2009 WL 10668158, at *26 (C.D. Cal. Jan. 16, 2009). Thus, a patentee **cannot** rely on material that is incorporated by reference from a provisional application to provide written description for a claim.

As discussed in detail below, the recitation of “a Delta-5 elongase gene under the control of a FAE promoter” lacks written description because the specification is completely devoid of any mention of a generic “FAE promoter.” The material that

PO relies on to support recitation of a “FAE promoter” is found solely in the provisional applications, which cannot be relied on for written description of the claims under 37 C.F.R. §1.57(d). Further, even the material incorporated by reference from the provisional applications does not provide written description for the genus of “FAE promoter” recited in the claims. The provisional applications do not recite the generic concept of an “FAE promoter.” Rather, the provisional applications only describe specific genetic constructs containing a **single species** of FAE promoter, the *Brassica napus* FAE1.1 promoter.¹⁰ There is no description in the provisional applications that supports the broad recitation of “a Delta-5 elongase gene under the control of a FAE promoter.” Ex. 1002, ¶88.

Further, as discussed below, the inventors were not in possession of *Brassica napus* seeds that comprise the full scope of amounts of ARA, EPA, and DHA recited in the claims. Ex. 1002, ¶89.

¹⁰ Further, the provisional applications only describe this *Brassica napus* FAE1.1 promoter joined to a specific nucleotide sequence d5Elo(Ot_GA3) (Table 13 of ‘622 Application).

2. Ground 1: No written description for a *Brassica napus* plant or part thereof comprising “a Delta-5 elongase gene under the control of a FAE promoter”

Independent claims 1 and 9 recite a *Brassica napus* plant or part thereof comprising “a Delta-5 elongase gene under the control of a FAE promoter.” However, the specification is completely devoid of *any* disclosure of “a Delta-5 elongase gene under the control of a FAE promoter.” Further, material incorporated by reference from the provisional applications cannot be relied upon to support written description of the claims unless the material also appears in the specification of the patent. Therefore, the description in the provisional applications of an *Ostreococcus tauri* Delta-5 elongase under the control of a *Brassica napus* FAE1.1 promoter *cannot* be relied upon provide written description for any claim, much less a claim directed to the broader concept of *any* Delta-5 elongase gene under the control of *any* “FAE promoter.” Ex. 1002, ¶90.

a. The ‘095 Patent does not describe any “FAE promoter” and PO cannot rely on description found solely in the provisional applications to provide written description of the claims

The specification of the ‘095 Patent does not mention, much less define or properly describe, a “FAE promoter” as recited in the claims. Ex. 1002, ¶91.

The Examples of the ‘095 Patent describe the fatty acid profiles and expression levels of plants transformed with genetic constructs named “VC-

LTM593-1qcz rc,” “VC-LJB2197-1qcz,” “VC-LLM337-1qcz rc,” “VC-LJB2755-2qcz rc,” and “VC-LLM391-2qcz rc.” Ex. 1001, 10:5-12. However, the full composition of these genetic constructs is ***not described at all*** in the ‘095 Patent. In fact, neither the term “FAE promoter” nor even “*Brassica napus* FAE1.1 promoter” appear anywhere in the specification of the ‘095 Patent. Only when referring to the description in the provisional applications could a POSITA determine that each genetic construct contains a specific $\Delta 5$ -elongase from *Ostreococcus tauri* under the control of the promoter of the “FAE1.1” gene from *Brassica napus*. Ex. 1002, ¶92.

Indeed, during prosecution of the ‘095 Patent, PO cited ***solely*** to disclosures in the provisional applications in their statement of support for the feature of “a Delta-5 elongase gene under the control of a FAE promoter.” See section V.C.1.e above. However, as discussed in section VIII.B.1, a patentee **cannot** rely on material that is incorporated by reference from a provisional application to provide written description for a claim. Accordingly, for this reason alone, the feature of “a Delta-5 elongase gene under the control of a FAE promoter” is ***new matter***, which does not have written description. Ex. 1002, ¶93.

b. The inventors were not in possession of Brassica napus plants comprising the genus of FAE promoters claimed

The term “FAE promoter,” is not recited or defined anywhere in the ‘095 Patent. However, as discussed in section VI.A, a POSITA would understand the

ordinary customary meaning of a “FAE promoter” to be any promoter that is naturally associated with a “Fatty Acid Elongation” or “Fatty Acid Elongase” gene in an organism. Ex. 1002, ¶94.

As noted in section V.B.1, above, even the provisional applications only describe specific genetic constructs containing a *Ostreococcus tauri* under the control of the promoter of the “FAE1.1” gene from *Brassica napus*. Neither the ‘095 Patent nor the provisional applications describe a genus of “FAE” promoter as recited in the claims. The disclosure of genetic constructs containing a specific $\Delta 5$ elongase gene under the control of a specific *Brassica napus* FAE1.1 promoter cannot be equated to a disclosure of any Delta-5 elongase gene under the control of any FAE promoter as recited in the claims. Ex. 1002, ¶95.

c. There is no written description in the specification of Brassica napus plants comprising a “FAE promoter” and the amounts of EPA, DHA, and ARA as claimed

Beyond the lack of description of an “FAE promoter” in the specification, there is no disclosure in the ‘095 Patent to suggest that the inventors intended to select, or in any way were in possession of, *Brassica napus* plants comprising a “Delta-5 elongase gene under the control of a FAE promoter” in combination with any of the following features recited in claim 1: (a) a content of EPA that is “at least 5% higher than of ARA”, (b) a content of EPA + DHA that is “at least 7% higher

than ARA”, or (c) a content of ARA that is “less than 4%,” a content of EPA that is more than 7%” and a content of DHA that is “more than 2%.” Ex. 1002, ¶96.

In the specification of the ‘095 Patent, the expression levels of the Delta-5 elongase during late stage seed development is highlighted as the cause of the claimed amounts of EPA, DHA and ARA. The specification asserts that “[t]he inventors have found that by carefully regulating the expression particularly of Delta-5 elongase activity it is possible to achieve the desired reduction in ARA lipids while maintaining ongoing synthesis of EPA and/or DHA.” Ex. 1001, 7:26-30. Ex. 1002, ¶97.

In particular, Example 4 of the specification notes that expression of the “Delta-5 elongase gene of the events LBFGKN and LBFLFK continued even after 30 days after flowering, whereas expression of the Delta-5 elongase gene of the events LANPMZ and LAODDN was severely reduced or only marginally detectable after 30 days of flowing.” Ex. 1001, 15:25-32. Example 5 notes that “only for events LBFGKN and LBFLFK a difference in EPA and ARA content of more than 5% could be achieved and a difference in (EPA+DHA) and ARA content of more than 7% could be achieved.” Ex. 1001, 16:43-49. Nowhere in the specification of the ‘095 Patent is any connection made between the use of a “FAE promoter” and the EPA, DHA, and ARA content of *Brassica napus* plants. Ex. 1002, ¶98.

Indeed, as discussed in section V.B.1, the *same Brassica napus* FAE1.1 promoter controlled expression of the Delta-5 elongase in *all* transgenic *Brassica napus* plants exemplified in the '095 Patent, *including* in *Brassica napus* plants that *did not* achieve (1) a difference in EPA and ARA content of more than 5%, or (2) a difference in (EPA+DHA) and ARA content of more than 7%. Therefore, a POSITA would understand that the presence of a Delta-5 elongase under the control of a FAE promoter is *not responsible* for maintenance or increase of Delta-5 elongase expression in late stage seed development, or the levels of EPA, ARA, and DHA recited in the claims. Ex. 1002, ¶99.

3. Ground 2: No written description of a *Brassica napus* plant or part thereof comprising lipids wherein “the content of EPA is at least 5% higher than of ARA”

a. The inventors were not in possession of the full scope of Brassica napus plants comprising lipids wherein “the content of EPA is at least 5% higher than of ARA”

Tables FA1, FA2, and FA3 of the '095 Patent summarize the ARA, EPA, and DHA contents of lipids obtained from seeds of *Brassica napus* plants of the transgenic events LANPMZ, LAODDN, LBFGKN and LBFLFK. Table FA4 shows the “composition of last lipids extract obtained for each event.” In event LBFGKN, at 45 days after flowering the amount of EPA was 7.6%, only 5.1% higher than the amount of ARA (2.5%). Table FA4 shows a difference of 5.17% in the “last lipids extract” of event LBFGKN. In event LBFLFK, at 46 days after flowering, the

amount of EPA was 8.6%, only 6.1% higher than the amount of ARA (2.5%). Table FA4 shows a difference of 6.03% in the “last lipids extract” of event LBFLFK. In the other two transgenic events, a 5% difference between the content of EPA and ARA was not achieved, with the LANPMZ event only achieving a difference of 2% at 46 days after flowering, and the LAODNN event only achieving a difference of 3.2% days after flowering.¹¹ As noted in the specification, “only for events LBFGKN and LBFLFK [could] a difference in EPA and ARA content of more than 5% [] be achieved.” Ex. 1001, 16:45-47. Ex. 1002, ¶100.

Notably, the **highest** difference between ARA and EPA content exemplified in the ‘095 Patent was in event LBFLFK, in which the level of EPA was **only 6.1% higher** than the level of ARA at 46 days after flowering. Despite the ‘095 Patent exemplifying *Brassica napus* plants comprising lipids wherein the content of EPA is at most 6.1% higher than the level of ARA, the claims encompass *Brassica napus* plants comprising lipids wherein the amount of EPA is 5% to 100% higher than of ARA. Ex. 1002, ¶101.

There is no disclosure in the ‘095 Patent regarding how to increase the difference between EPA and ARA levels beyond the amounts produced in transgenic

¹¹ Table FA4 shows a difference between EPA and ARA of 1.96% and 3.28% in the last lipids extracts of events LANPMZ and LAODNN, respectively

events LBFGKN and LBFLFK. Thus, based on the examples of the ‘095 Patent, a POSITA could not reasonably conclude that the inventors had possession of the genus of *Brassica napus* plants comprising 5% to 100% more EPA than ARA. Ex. 1002, ¶102.

b. The claims do not recite, and the ‘095 Patent fails to describe, the structures necessary to achieve the claimed lipid levels in a Brassica napus plant

As discussed in section V.A.2, the specification of the ‘095 Patent asserts that a reduction in ARA lipids and increase in EPA is achieved through the use of “a Delta-5 elongase gene under the control of a promoter such that expression of the Delta-5 elongase gene is maintained or increased in late stage seed development.” Ex. 1001, 7:26-30. Ex. 1002, ¶103.

However, as discussed in section V.D, the data in the ‘095 demonstrate that a “FAE promoter” is ***not*** responsible for causing maintained or increased expression of a Delta-5 elongase during late stage seed development because ***all*** plants exemplified in the ‘095 Patent included a Delta-5 elongase under the control of the same FAE1.1 promoter from *Brassica napus*, including plants in which Delta-5 elongase expression was not maintained or increased in late stage seed development. Thus, neither the differences in Delta-5 elongase expression, nor the differences in EPA and ARA levels of the different events described in the ‘095 Patent can be explained by use of a “FAE promoter” as recited in the claims. Ex. 1002, ¶104.

4. **Ground 3: No written description of a *Brassica napus* plant or part thereof comprising lipids wherein “the sum of contents of EPA+DHA is at least 7% higher than ARA”**

a. *The inventors were not in possession of the full scope of Brassica napus plants comprising lipids wherein “the sum of contents of EPA+DHA is at least 7% higher than ARA”*

Tables FA1 through FA4 of the specification show that the **highest** difference between ARA and EPA content exemplified in the ‘095 Patent was in event LBFLFK, in which the level of EPA+DHA was only 9.64% higher than the level of ARA. The second highest difference was achieved in event LBFGKN, at a difference in the last lipids extract of 7.56%. Neither of the other events reached the minimum claimed difference of “at least 7%,” with event LANPMZ only achieving a difference of 4.96% and event LAODDN only achieving a difference of 5.74%. As noted in the specification, “only for events LBFGKN and LBFLFK [could] [...] a difference in (EPA+DHA) and ARA content of more than 7% [] be achieved.” Ex. 1001, 16:45-47. Ex. 1002, ¶105.

Despite the ‘095 Patent exemplifying *Brassica napus* plants comprising lipids wherein the content of EPA+DHA is **at most 9.64% higher** than the level of ARA, the claims encompass *Brassica napus* plants comprising lipids wherein the amount of EPA+DHA is 7% to 100% higher than of ARA. There is no disclosure in the ‘095 Patent regarding how to increase the difference between EPA+DHA and ARA levels

beyond the amounts produced in transgenic events LBFGKN and LBFLFK. Thus, based on the examples of the '095 Patent, a POSITA could not reasonably conclude that the inventors had possession of the genus of *Brassica napus* plants comprising 7% to 100% more EPA+DHA than ARA. Ex. 1002, ¶106.¹²

b. The '095 Patent fails to describe the structures necessary to achieve the claimed lipid levels in a Brassica napus plant

As discussed above, the specification of the '095 Patent asserts that a reduction in ARA lipids and increase in EPA and DHA is achieved through the use of “a Delta-5 elongase gene under the control of a promoter such that expression of the Delta-5 elongase gene is maintained or increased in late stage seed development.” Ex. 1001, 7:26-30. However, the data in the '095 demonstrate that a “FAE promoter” is **not** responsible for causing maintained or increased expression of a Delta-5 elongase during late stage seed development because **all** plants exemplified in the '095 Patent included a Delta-5 elongase under the control of the same FAE1.1 promoter from *Brassica napus*, including plants in which expression

¹² Further the claims that recite that EPA+DHA that is 7% higher than ARA encompass plants or parts thereof comprising 7-100% DHA and 0% EPA, or 0% DHA and 7-100% EPA. As discussed below, the inventors were not in possession of these amounts of EPA or DHA. See Ex. 1002, ¶110-111.

of the Delta-5 elongase expression was not maintained or increased in late stage seed development. Thus, neither the differences in Delta-5 elongase expression, nor the differences in EPA+DHA and ARA levels of the different events described in the '095 Patent can be explained by use of a "FAE promoter." Ex. 1002, ¶107.

5. Ground 4: No written description of a *Brassica napus* plant or part thereof comprising lipids wherein "the content of ARA is less than 4% and the content of EPA is more than 7% and the content of DHA is more than 2%"

a. The inventors were not in possession of the full scope of Brassica napus plants comprising lipids wherein "the content of ARA is less than 4% and the content of EPA is more than 7% and the content of DHA is more than 2%"

The claims encompass far more than transgenic *Brassica napus* plants having an ARA content of less than 4%, a content of EPA of 7%, and a content of DHA of 2%. The claims encompass transgenic *Brassica napus* plants with 0-4% ARA, 7-98% EPA, and 2-93% DHA. Ex. 1002, ¶108.

Table FA4 of the '095 Patent shows that only plants from two of the four transgenic events produced by the inventors achieved levels within the claimed scope of 0-4% ARA, 7-98% EPA, and 2-93% DHA. The highest level of EPA and DHA achieved in *any* *Brassica napus* plant produced by the inventors was in plants from event LBFLFK. In plants from this event, the level of EPA in last lipids was 8.57%, the level of DHA was 3.61%, and the level of ARA was 2.54%. Event

LBFGKN reached a level of EPA of 7.64%, a level of DHA of 2.39%, and a level of ARA of 2.47%. Neither of the other events reached even the minimum of the claimed range for EPA and DHA. Ex. 1002, ¶109.

Based on this data, a POSITA would not reasonably conclude that the inventors had possession of the genus of 0-4% ARA, 7-98% EPA, and 2-93% DHA in lipids of seeds from *Brassica napus*. In particular, in plants that reached the minimum required levels of EPA and DHA, the lowest amount of ARA achieved was 2.47%. A POSITA would not reasonably conclude that the inventors were in possession of plants comprising even the minimum level of EPA of 7%, the minimum level of DHA of 2%, and an ARA level close to or approaching 0%. Ex. 1002, ¶110.

Conversely, the very highest levels of EPA and DHA achieved in the '095 Patent were 8.57% and 3.61%, respectively, close to the very bottom of the ranges encompassed by the claims (7-98% for EPA and 2-93% DHA.) Based on this data, a POSITA would not reasonably conclude that the inventors were in possession of plants comprising up to 98% EPA or up to 93% DHA. Further, because the maximum difference between EPA+DHA and ARA achieved in any plant was 9.64%, a POSITA would not reasonably conclude that the inventors were in possession of a plant with an ARA level of less than 4% and EPA+DHA levels much higher than the amounts exemplified in events LBFLFK and LBFGKN (for example

30%, which would be well within the scope of the range encompassed by the claims).

Ex. 1002, ¶111.

6. Ground 5: No written description of a *Brassica napus* plant “wherein the content of EPA in the lipids of the seeds increases at least 1.0% by weight of total lipids during late stage seed development”

a. The inventors were not in possession of the full scope of Brassica napus plants “wherein the content of EPA in the lipids of the seeds increases at least 1.0% by weight of total lipids during late stage seed development”

The claims encompass far more than transgenic *Brassica napus* plants wherein the content of EPA in the lipids of the seeds increases at least 1.0% by weight of total lipids during late stage seed development. The claims encompass *Brassica napus* plants wherein the content of EPA in the lipids of the seeds increases 1-100% by weight of total lipids during late stage seed development. Ex. 1002, ¶112.

The ‘095 Patent does not define late stage seed development. Nevertheless, based on the ordinary and customary meaning of the term, a POSITA might understand the term to refer to the period starting approximately 30 days after flowering. Ex. 1002, ¶113.

In the ‘095 Patent, only plants from events LBFGKN and LBFLFK exhibited an increase in the content of EPA of at least 1% in late-stage seed development. Plants from event LBFGKN exhibited an increase in EPA from day 31 to day 45

after flowering of 1.5%, while plants from event LBFLFK exhibited an increase in EPA from day 31 to 46 after flowering of 1.1%. Ex. 1002, ¶114.

Based on this data, a POSITA would not reasonably conclude that the inventors had possession of the full scope of *Brassica napus* plants wherein the content of EPA in the lipids of the seeds increases 1-100% in late stage seed development. Ex. 1002, ¶115.

b. The ‘095 Patent fails to describe the structures necessary to achieve the claimed increase in EPA level during late stage seed development

As discussed in section V.A.2, the specification of the ‘095 Patent asserts that a reduction in ARA lipids and increase in EPA is achieved through the use of “a Delta-5 elongase gene under the control of a promoter such that expression of the Delta-5 elongase gene is maintained or increased in late stage seed development.” Ex. 1001, 7:26-30. However, as discussed in section V.D, the data in the ‘095 demonstrate that a “FAE promoter” is *not* responsible for causing maintained or increased expression of a Delta-5 elongase during late stage seed development because *all* plants exemplified in the ‘095 Patent included a Delta-5 elongase under the control of the same FAE1.1 promoter from *Brassica napus*, including plants which did not exhibit an increase in EPA content of at least 1% in late-stage seed development, and in which Delta-5 elongase expression was not maintained or increased in late-stage seed development. Ex. 1002, ¶116.

Thus, neither the difference in Delta-5 elongase expression, nor the increase in EPA content in late-stage seed development can be explained by use of a “FAE promoter.” Ex. 1002, ¶117.

7. Ground 6: No written description of the full scope of “harvesting the plants or a part thereof when the lipids content of ARA in the lipids of the seeds has decreased”

a. Claims 3-4 encompass harvesting plants or a part thereof when the lipids content of ARA has decreased to 0%

Claim 3 recites a “[m]ethod of producing a Brassica napus plant seed lipid composition, comprising the steps of a) growing Brassica napus plants according to claim 1, b) harvesting the plants or a part thereof when the lipids content of ARA in the lipids of the seeds has decreased.” Claim 4 further specifies “wherein ARA in the lipids of the seeds decreases by at least 0.5 wt.-%.” Ex. 1002, ¶118.

Such claims encompass harvesting the plants or a part thereof when the lipids content of ARA has decreased by *any* amount, including a decrease in ARA content to 0% by weight. Ex. 1002, ¶119.

b. The inventors were not in possession of a decrease in ARA content to 0% by weight

Table FA1 of the ‘095 Patent shows the ARA level in lipids of seeds from the four different transgenic events exemplified in the application. In three of the events, the level of ARA decreases slightly starting around 35 days after flowering. In seeds from event LAODDN, the level of ARA decreases by only 0.2% by weight from

1.5% at the peak level to 1.3%, and in seeds from event LBFGKN, the level of ARA decreases by only 0.5% from 3.0% at the peak level to 2.5%. The ***greatest decrease in level of ARA*** is found in seeds of event LBFLFK, which ***decrease by 0.8%*** by weight from 3.3% at the peak level to 2.5%. Based on this data, a POSITA would not conclude that the inventors had possession of a step of harvesting the plants or a part thereof when the lipids content of ARA in the lipids of the seeds has decreased to 0% by weight. Because the claims encompass decreases in ARA levels by amounts greater than 0.8% by weight and encompass a reduction to 0% by weight the inventors were not in possession of the full scope of the invention recited in claims 3 and 4. Ex. 1002, ¶120.

C. Grounds 7-11: The claims are not enabled

1. Legal standard for enablement

To meet the enablement requirement of 35 U.S.C. § 112, the disclosure must teach a POSITA how to make and use the full scope of the claimed invention without “undue experimentation.” *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997) (citing *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988)).

Factors to be considered in determining whether undue experimentation is required include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of

those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). However, a court need not consider all these factors when determining whether a disclosure is enabling. *See Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1371 (Fed. Cir. 1999). What matters for the purpose of the enablement inquiry are the particular facts being considered. *See Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1213 (Fed. Cir. 1991).

A specification that “provides a starting point from which one of skill in the art can perform further research in order to practice the claimed invention” does not fulfill the enablement requirement. *Nat’l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1198 (Fed. Cir. 1999) “Th[e] important [enablement] doctrine prevents both inadequate disclosure of an invention and overbroad claiming that might otherwise attempt to cover more than was actually invented. Thus, a patentee chooses broad claim language at the peril of losing any claim that cannot be enabled across its full scope of coverage.” *MagSil Corp. v. Hitachi Global Storage Techs., Inc.*, 687 F.3d 1377, 1381 (Fed. Cir. 2012). “Enabling the full scope of each claim is ‘part of the quid pro quo of the patent bargain.’ . . . A patentee who chooses broad claim language must make sure the broad claims are fully enabled.” *Sitrick v. Dreamworks, LLC*, 516 F.3d 993, 999 (Fed. Cir. 2008). “When a range is claimed, there must be reasonable enablement of

the scope of the range.” *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003).

The disclosure of the ‘095 Patent does not teach a POSITA how to make and use the full scope of the claimed invention without undue experimentation. As discussed in detail below, the claims encompass broad ranges of levels of EPA, and DHA while only some plants produced by the inventors had levels of EPA and DHA within the scope of the claims, barely achieving the bottom end of the claimed ranges. Conversely, the claims encompass plants with high levels of EPA and DHA and as low as zero ARA while the plants produced by the inventors all had levels of ARA well above zero. Further, the specification is devoid of any concrete guidance regarding modifications that could be made to further increase the levels of DHA and EPA and decrease the levels of ARA beyond what was exemplified. Accordingly, the disclosure does not teach the POSITA how to make and use the full claimed scope, without undue experimentation. Ex. 1002, ¶121.

2. Ground 7: A *Brassica napus* plant or part thereof comprising lipids wherein “the content of EPA is at least 5% higher than of ARA” is not enabled across its full scope

The specification of the ‘095 Patent does not teach a POSITA how to make and use a transgenic *Brassica* plant which produces lipids comprising a content of EPA that “is at least 5% higher than of ARA” without undue experimentation. Ex. 1002, ¶122.

a. The claims encompass Brassica napus plants comprising a wide range of levels of EPA and ARA

The claims encompass more than *Brassica napus* lipids comprising a content of EPA that is 5% higher than of ARA. The claims encompass *Brassica napus* lipids where the content of EPA is between 5% and over 90% higher than of ARA. “When a range is claimed, there must be reasonable enablement of the scope of the range.” *AK Steel v. Sollac*, 344 F.3d at 1244. Ex. 1002, ¶123.

The Federal Circuit’s decision on an open-ended range in *MagSil*, 687 F.3d 1377 is directly relevant here. In *MagSil*, like the claims here, the patent claimed a “tunnel junction device” wherein “applying a small magnitude of electromagnetic energy to the junction . . . causes a change in the resistance by at least 10% at room temperature.” *Id.* at 1381 (emphasis added). The district court construed the “at least 10%” limitation to cover “resistance changes beyond 120% and up to infinity.” *Id.* The district court invalidated the patent on summary judgment for lack of enablement because the patent did not teach one of skill in the art how to perform the method across the full scope of the claim.

In affirming the district court, the Federal Circuit emphasized that “[t]he specification. . . [taught] that the inventors’ best efforts achieved a maximum change in resistance of only 11.8% at room temperature,” only reaching the lower end of the claimed scope. *Id.* at 1381..

The claim term “the content of EPA is at least 5% higher than of ARA” is very similar to the “open-ended” “at least 10%” term in *Magsil* because the term has a lower threshold, but no recited upper limit. In *Magsil*, the court invalidated claims that were only enabled at the lower end of the claimed scope. Claims 1-6 and 8 of the ‘095 Patent recite and encompass lipids from *Brassica napus* where the level of EPA is between 5% and 100% higher than of ARA. Claim 7 recites a minimum level of DHA of 2%, therefore encompassing lipids from *Brassica napus* where the level of EPA is between 5% and 98% higher than of ARA. By contrast, the greatest difference in level of EPA and ARA exemplified in the ‘095 Patent is 6.03%, barely meeting the minimum difference recited in these claims. Ex. 1002, ¶124.

b. The ‘095 Patent does not provide any meaningful guidance regarding how to achieve a content of EPA that is at least 5-98% higher than of ARA

The ‘095 Patent is also devoid of disclosure of how to reliably achieve a content of EPA that is, for example, 10% higher than of ARA, let alone 20%, 30%, or 40+% higher than of ARA as encompassed by the claims. As discussed in section V.A.2.a, the specification attributes the difference in EPA and ARA levels to “a Delta-5 elongase gene under the control of a promoter such that expression of the Delta-5 elongase gene is maintained or increased in late stage seed development.” However, the specification does not describe any such promoter. As discussed in V.B.1, a *Brassica napus* FAE1.1 promoter was used in *all* plants exemplified in the

‘095 Patent, including plants which *did not* achieve a 5% difference between level of EPA and ARA and which *did not* exhibit the expression profile that the inventors credit for producing a 5% difference between EPA and ARA levels. Based on this disclosure, it is clear that a person of skill in the art could not make and use the full scope of the claimed invention without undue experimentation. Ex. 1002, ¶125.

3. Ground 8: A *Brassica napus* plant or part thereof comprising lipids wherein “the sum of contents of EPA+DHA is at least 7% higher than ARA” is not enabled across its full scope

The specification of the ‘095 Patent does not teach a POSITA how to make and use a transgenic *Brassica* plant comprising a content of EPA+DHA that “is at least 7% higher than of ARA” without undue experimentation. Ex. 1002, ¶126.

a. The claims encompass *Brassica napus* plants comprising a wide range of levels of EPA, DHA and ARA

The claims encompass more than *Brassica napus* lipids comprising a content of EPA+DHA that is 7% higher than of ARA. The claims encompass *Brassica napus* lipids where the content of EPA+DHA is between 7% and 90+% higher than of ARA. “When a range is claimed, there must be reasonable enablement of the scope of the range.” *AK Steel v. Sollac*, 344 F.3d at 1244. *See also MagSil*, 687 F.3d 1377. The greatest difference in level of EPA+DHA and ARA exemplified in the ‘095

Patent is 9.64%, barely meeting the minimum difference recited in these claims.

Ex. 1002, ¶127.¹³

b. The ‘095 Patent does not provide any meaningful guidance regarding how to achieve a content of EPA+DHA that is at least 7% higher than of ARA

The ‘095 Patent is also devoid of disclosure of how to reliably achieve a content of EPA+DHA that is, for example, 15% higher than of ARA, let alone 20%, 30%, or 40+% higher than of ARA as encompassed by the claims. As discussed in section V.A.2.a, the specification attributes the difference in EPA+DHA and ARA levels to “a Delta-5 elongase gene under the control of a promoter such that expression of the Delta-5 elongase gene is maintained or increased in late stage seed development.” However, the specification does not describe any such promoter. As discussed in V.B.1, a *Brassica napus* FAE1.1 promoter was used in *all* plants exemplified in the ‘095 Patent, including plants which ***did not*** achieve a 5% difference between level of EPA and ARA and which ***did not*** exhibit the expression profile that the inventors credit for producing a 5% difference between EPA+DHA

¹³ Further the claims that recite that EPA+DHA that is 7% higher than ARA encompass plants or parts thereof comprising 7-100% DHA and 0% EPA, or 0% DHA and 7-100% EPA. As discussed below, the specification clearly does not enable these amounts of EPA or DHA. *See* Ex. 1002, ¶133.

and ARA levels. Based on this disclosure, it is clear that a person of skill in the art could not make and use the full scope of the claimed invention without undue experimentation. Ex. 1002, ¶128.

4. Ground 9: A *Brassica napus* plant or part thereof comprising lipids wherein “the content of ARA is less than 4% and the content of EPA is more than 7% and the content of DHA is more than 2%” is not enabled across its full scope

The specification of the ‘095 Patent does not teach a POSITA how to make and use a transgenic *Brassica* plant which produces lipids comprising the content of ARA is less than 4% and the content of EPA is more than 7% and the content of DHA is more than 2%. Ex. 1002, ¶129.

a. *The claims encompass Brassica napus plants comprising a wide range of levels of EPA, DHA and ARA*

The claims encompass more than *Brassica napus* lipids comprising 7% EPA, 2% DHA and 4% ARA. The claims encompass *Brassica napus* lipids where the level of EPA is between 7% and 98%, the level of DHA is between 2% and 93% and the level of ARA is between 0% and 4%. “When a range is claimed, there must be reasonable enablement of the scope of the range.” *AK Steel v. Sollac*, 344 F.3d at 1244. *See also MagSil*, 687 F.3d 1377 Ex. 1002, ¶130.

The greatest level of EPA exemplified in the ‘095 Patent is 8.57%, while the greatest level of DHA exemplified in the ‘095 Patent is 3.61%, each amount barely meeting the minimum levels recited in the claims and far from the maximum levels

of 98% and 93% encompassed by the claims. Similarly, the lowest level of ARA exemplified in a *Brassica napus* plant with at least 7% EPA and 2% DHA was 2.47%, far from the minimum of 0% encompassed by the claims. Ex. 1002, ¶131.

b. The ‘095 Patent does not provide any meaningful guidance regarding how to achieve a content of EPA that is more than 7% and a content of DHA that is more than 2%

The specification of the ‘095 Patent notes that one intermediate in the production of EPA and DHA generally is ARA. Ex. 1001, 1:57-59. The specification of the ‘095 Patent further notes that because ARA is an intermediate in the production of DHA “and because [ARA] can be converted by omega-3 desaturases to and from EPA, it is generally not possible to avoid concomitant production of [ARA] in transgenic plant metabolism” Ex. 1001, 1:59-63. Ex. 1002, ¶132.

Despite these noted difficulties in increasing levels of EPA and DHA without also increasing levels of ARA in transgenic plant metabolism, the ‘095 Patent is devoid of disclosure of how to reliably achieve a content of EPA that is, for example, 15% by weight, let alone 20%, 30%, or 40+% as encompassed by the claims. Further, the ‘095 Patent is devoid of disclosure of how to reliably achieve a content of DHA that is, for example, 5% by weight, let alone 10%, 20%, or 30+% as encompassed by the claims. Still further, the ‘095 Patent is devoid of disclosure of

how to achieve of content of ARA that is less than 2%, let alone 1% or 0% as encompassed by the claims. Ex. 1002, ¶133.

Based on this lack of disclosure, it is clear that a POSITA could not make and use the full scope of the claimed invention without undue experimentation. Ex. 1002, ¶134.

5. **Ground 10: A *Brassica napus* plant wherein, when the *Brassica napus* plant or part thereof is grown, the content of ARA in the lipids of the seeds decreases at least 0.5% by weight of total lipids and the content of EPA and/or DHA in the lipids of the seeds increases is not enabled across its full scope**

Claims 9-11 recite a *Brassica napus* plant wherein “when the *Brassica napus* plant or part thereof is grown, the content of ARA in the lipids of the seeds decreases at least 0.5% by weight of total lipids and the content of EPA and/or DHA in the lipids of the seeds increases.” Ex. 1002, ¶135.

- a. ***The claims encompass a wide range of increases in content of EPA and/or DHA and a wide range of decreases in the content of ARA***

The claims encompass more than *Brassica napus* wherein the content of ARA in the lipids of the seeds decreases 0.5% by weight, and wherein the content of EPA and/or DHA in the lipids of the seeds increases. The claims encompass *Brassica napus* wherein the content of ARA in the lipids of the seeds decreases to 0% by weight and wherein EPA and/or DHA increase to 100% by weight. To achieve such

increases in EPA and DHA and decreases in ARA would require a **complete** conversion of shorter chain fatty acids through ARA and then to EPA and DHA. The ‘095 Patent provides no evidence that such a complete conversion is achievable based on its disclosure. Ex. 1002, ¶136.

b. The ‘095 Patent does not provide any meaningful guidance regarding how to achieve an increase in the content EPA and/or DHA when a Brassica napus plant is grown

As discussed in section V.A.2.a, the specification attributes the difference in EPA, DHA and ARA levels to “a Delta-5 elongase gene under the control of a promoter such that expression of the Delta-5 elongase gene is maintained or increased in late stage seed development.” However, the specification does not describe any such promoter. As discussed in V.B.1, a *Brassica napus* FAE1.1 promoter was used in **all** plants exemplified in the ‘095 Patent, including plants which **did not** achieve a 5% difference between level of EPA and ARA and which **did not** exhibit the expression profile that the inventors credit for producing a 5% difference between EPA, DHA and ARA levels. Because the ‘095 Patent attributes the claimed levels of EPA, DHA and ARA to a particular expression profile of the Delta-5 elongase gene but does not describe any promoter which can be reliably used to achieve this expression profile, a POSITA would be left to undue experimentation to identify such a promoter. Further, based on the data in the ‘095 Patent showing a

maximum level of EPA of 8.57%, a maximum level of DHA of 3.61%, and an ARA level of 2.54%, even if the expression profile of the Delta-5 elongase could reliably be achieved, it could not be used to produce *Brassica napus* plants where the ARA level decreases to 0% and the EPA and/or DHA level increases to 100% as encompassed by the claims. Ex. 1002, ¶137.

6. Ground 11: A *Brassica napus* plant “wherein the content of EPA in the lipids of the seeds increases at least 1.0% by weight of total lipids during late stage seed development”

Claims 10 recite a *Brassica napus* plant “wherein the content of EPA in the lipids of the seeds increases at least 1.0% by weight of total lipids during late stage seed development.” Ex. 1002, ¶138.

a. The claims encompass a wide range of increases in content of EPA and/or DHA and a wide range of decreases in the content of ARA

The claims encompass more than *Brassica napus* wherein the content of EPA in the lipids of the seeds increases at least 1.0% during late stage seed development. The claims encompass *Brassica napus* wherein the content of EPA in the lipids of the seeds increases 1-100%, to a level of 100% during late stage seed development. Such an increase is clearly not enabled. “When a range is claimed, there must be reasonable enablement of the scope of the range.” *AK Steel v. Sollac*, 344 F.3d at 1244. *See also MagSil*, 687 F.3d 1377 Ex. 1002, ¶139.

The greatest increase in EPA level in late stage seed development exemplified in the '095 Patent is in event LBFLFK, which increased from 7.5% to 8.6% in late stage seed development. This represents an increase of only 1.1%, barely meeting the minimum increase recited in the claims and far from the maximum increase of 100% encompassed by the claims. Ex. 1002, ¶140.

b. The '095 Patent does not provide any meaningful guidance regarding how to achieve an increase in the content EPA in late stage seed development

The '095 Patent is devoid of disclosure of how to achieve an increase in EPA content of 2%, 3%, 5%, 10%, or 20+% as encompassed by the claims. As discussed in section V.A.2.a, the specification attributes the EPA levels of the claimed *Brassica napus* plants to “a Delta-5 elongase gene under the control of a promoter such that expression of the Delta-5 elongase gene is maintained or increased in late stage seed development.” However, the specification does not describe any such promoter. As discussed in V.B.1, a *Brassica napus* FAE1.1 promoter was used in *all* plants exemplified in the '095 Patent, including plants which ***did not*** achieve a 1% increase in EPA content in late stage seed development and which ***did not*** exhibit the expression profile that the inventors credit for producing a *Brassica napus* plants with EPA levels that increase in late stage seed development. Based on this disclosure, it is clear that a person of skill in the art could not make and use the full scope of the claimed invention without undue experimentation. Ex. 1002, ¶141.

7. Ground 12: Lack of enablement of the full scope of “harvesting the plants or a part thereof when the lipids content of ARA in the lipids of the seeds has decreased”

a. Claims 3-4 encompass harvesting plants or a part thereof when the lipids content of ARA has decreased to 0%

Claim 3 recites a “[m]ethod of producing a Brassica napus plant seed lipid composition, comprising the steps of a) growing Brassica napus plants according to claim 1, b) harvesting the plants or a part thereof when the lipids content of ARA in the lipids of the seeds has decreased.” Claim 4 further specifies “wherein ARA in the lipids of the seeds decreases by at least 0.5 wt.-%.” Ex. 1002, ¶142.

Such claims encompass harvesting the plants or a part thereof when the lipids content of ARA has decreased by *any* amount, including a complete elimination of ARA to a content of 0% by weight. Ex. 1002, ¶143.

b. The specification does not enable a decrease in ARA content to 0% by weight

Table FA1 of the ‘095 Patent shows the ARA level in lipids of seeds from the four different transgenic events exemplified in the application. In three of the events, the level of ARA decreases slightly starting around 35 days after flowering. In seeds from event LAODDN, the level of ARA decreases by only 0.2% by weight from 1.5% at the peak level to 1.3%, and in seeds from event LBFGKN, the level of ARA decreases by only 0.5% from 3.0% at the peak level to 2.5%. The *greatest* decrease

in level of ARA is found in seeds of event LBFLFK, which decrease by 0.8% by weight from 3.3% at the peak level to 2.5%. Ex. 1002, ¶144.

Based on this data, it is clear that a person of skill in the art would not be able to practice step of harvesting the plants or a part thereof when the lipids content of ARA in the lipids of the seeds has decreased to 0% by weight without undue experimentation. Because the claims encompass decreases in ARA levels by amounts greater than 0.8% by weight and encompass a reduction to 0% by weight, the '095 Patent does not enable the full scope of the invention recited in claims 3 and 4. Ex. 1002, ¶145.

D. Grounds 13-14: The claims are anticipated

1. Ground 13: Claims 1 and 6 are anticipated by PCT International Patent Application Publication No. WO 2013/185184

PCT International Application Publication No. WO 2013/185184 (“the ‘184 publication”, Ex. 1013), published December 19, 2013, before the November 13, 2015 filing date of PCT International Application No. PCT/EP2015/076630 and before the filing date of both provisional application to which the ‘095 Patent claims priority. Ex. 1002, ¶146.

a. Disclosure of the WO 2013/185184

The '184 publication describes, *inter alia*, the transformation of *Brassica napus* plants with constructs which cause the production of ARA, EPA, and DHA within the scope of the claims as discussed below. Ex. 1002, ¶147.

b. Claims 1-8 are anticipated by the WO 2013/153404

<u>Claim</u>	<u>Claim element</u>	<u>Disclosure in WO 2013/185184</u>
1	Brassica napus plant or part thereof,	Example 4 describes <i>B. napus</i> plants. Ex. 1013, pp. 118-121
1	comprising seeds that comprise lipids including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and optionally arachidonic acid (ARA), wherein	The seeds of the <i>B. napus</i> plants described in Example 4 comprised seeds that comprise EPA (20:5ω3), and DHA (22:6ω3). Ex. 1013, pp. 121
1	<p>a) the content of EPA is at least 5% higher than of ARA, and/or</p> <p>b) the sum of contents of EPA+DHA is at least 7% higher than ARA and/or</p> <p>c) the content of ARA is less than 4% and the content of EPA is more than 7% and the content of DHA is more than 2%,</p>	Line CT125-2 #10 (far right column) of Table 13 has 0.3% (20:5ω3), and 8.5% DHA (22:6ω3). These lines did not contain ARA. Ex. 1013, p. 121. Therefore, the sum of the contents of EPA+DHA is at least 7% higher than of ARA in these T2 seeds.

<u>Claim</u>	<u>Claim element</u>	<u>Disclosure in WO 2013/185184</u>
1	and wherein the Brassica napus plant or part thereof comprises a Delta-5 elongase gene under the control of a FAE promoter.	The “GA7 construct” used to transform the seed whose fatty acid profile is shown in Table 13 comprise a Delta-5 elongase gene under the control of a FAE promoter. Ex. 1013, pp. 40 and 189 (Figure 2).
6,	The Brassica napus plant or part thereof of claim 1,	See above for limitations of claim 1
6	wherein the sum of contents of EPA+DHA is at least 7% higher than ARA in the lipids of the seeds.	Line CT125-2 #10 (far right column) of Table 13 has 0.3% (20:5ω3), and 8.5% DHA (22:6ω3). These lines did not contain ARA. Ex. 1013, p. 121. Therefore, the sum of the contents of EPA+DHA is at least 7% higher than of ARA in these T2 seeds.

Ex. 1002, ¶147.

2. Ground 14: Claims 1 and 6 are anticipated by PCT International Application Publication No. WO 2015/089587

PCT International Application Publication No. WO 2015/089587 (“the ‘587 publication”, Ex. 1014), published June 25, 2015, before the November 13, 2015 filing date of PCT International Application No. PCT/EP2015/076630. Ex. 1002, ¶148.

As discussed in section V.B, many of the concepts recited in the claims of the ‘095 Patent are entirely absent from either provisional application to which the Patent claims priority. Although Petitioner maintains that the claims of the ‘095 Patent are not described or enabled even in PCT International Application

No. PCT/EP2015/076630, to the extent claims of the ‘630 Patent are found to be enabled and described in PCT International Application No. PCT/EP2015/076630, they are anticipated by the ‘587 publication. Ex. 1002, ¶149.

a. Disclosure of the WO 2015/089587

The ‘587 publication describes, *inter alia*, the transformation of *Brassica napus* plants with constructs which cause the production of ARA, EPA, and DHA within the scope of the claims as discussed below. Ex. 1002, ¶150.

b. Claims 1 and 6 are anticipated by the WO 2015/089587

<u>Claim</u>	<u>Claim element</u>	<u>Disclosure in WO 2015/089587</u>
1	Brassica napus plant or part thereof,	Example 4 describes <i>B. napus</i> plants. Ex. 1014, p. 117.
1	comprising seeds that comprise lipids including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and optionally arachidonic acid (ARA), wherein	The seeds of the <i>B. napus</i> plants described in Example 4 comprised seeds that comprise EPA (C20:5n3), and DHA (C22:6n3). Ex. 1014, p. 122.
1	a) the content of EPA is at least 5% higher than of ARA, and/or b) the sum of contents of EPA+DHA is at least 7% higher than ARA and/or	All T2 seeds whose fatty acid profiles are shown in Table 10—except CT136-27-18-6 and CT136-27-18-9—had a DHA (C22:6n3) level in excess of 7%. Ex. 1014, p. 122. No ARA was detected in any of the samples. Ex. 1014, p. 122, third line from bottom. Therefore, the sum of the contents of EPA+DHA is at least 7% higher than of ARA in these T2 seeds.

<u>Claim</u>	<u>Claim element</u>	<u>Disclosure in WO 2015/089587</u>
	c) the content of ARA is less than 4% and the content of EPA is more than 7% and the content of DHA is more than 2%,	
1	and wherein the Brassica napus plant or part thereof comprises a Delta-5 elongase gene under the control of a FAE promoter.	The “modB construct” in the <i>B. napus</i> seeds whose fatty acid profiles are shown in Table 10 includes a Delta-5 elongase under the control of an Arabidopsis FAE1 promoter. Ex. 1014, pp. 44 and 179 (Figure 2).
6	The Brassica napus plant or part thereof of claim 1,	See above for limitations of claim 1
6	wherein the sum of contents of EPA+DHA is at least 7% higher than ARA in the lipids of the seeds.	All T2 seeds whose fatty acid profiles are shown in Table 10—except CT136-27-18-6 and CT136-27-18-9—had a DHA (C22:6n3) level in excess of 7%. Ex. 1014, p. 122. No ARA was detected in any of the samples. Ex. 1014, p. 122, third line from bottom. Therefore, the sum of the contents of EPA+DHA is at least 7% higher than of ARA in these T2 seeds.

Ex. 1002, ¶150.

IX. CONCLUSION

For all the foregoing reasons, it is more likely than not that claims 1-3 of the ‘095 Patent are unpatentable. Accordingly, the Board should institute post-grant review of claims 1-11 of the ‘095 Patent.

Petition for Post-Grant Review
of U.S. Patent No. 11,260,095

Respectfully submitted,

/Gary J. Gershik/

Dated: November 30, 2022

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CERTIFICATE OF COMPLIANCE WITH TYPE VOLUME LIMITATION

Pursuant to 37 C.F.R. § 42.24(d), I hereby certify that this Petition complies with the type-volume limitation of 37 C.F.R. § 42.24(a)(1)(ii) because, based upon the word count of the word-processing system used to prepare this petition, the number of words in this petition is 17,151. Pursuant to 37 C.F.R. §42.24(a), this word count does not include “a table of contents, a table of authorities, mandatory notices under § 42.8, a certificate of service or word count, or appendix of exhibits or claim listing.”

By: /Darren Haber/

Dated: November 30, 2022

Darren Haber

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH
ORGANISATION,
Petitioner,

v.

BASF PLANT SCIENCE GMBH,
Patent Owner.

U.S. Patent No. 11,260,095

Issued: March 1, 2022

CERTIFICATE OF SERVICE

I hereby certify that the foregoing PETITION FOR POST-GRANT REVIEW, EXHIBITS 1001-1015, and COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANISATION'S POWER OF ATTORNEY were served this 30th day of November 2022 by e-mail to Marshall, Gerstein & Borun LLP, the attorneys of record for the Patent Owner, who have agreed to accept service electronically at the email addresses listed below:

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