

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

**DECLARATION OF NARENDRA YADAV, Ph.D.,
IN SUPPORT OF PETITION FOR POST-GRANT REVIEW
OF U.S. PATENT NO. 11,260,095**

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I, Narendra Yadav, Ph.D., hereby declare as follows:

I. INTRODUCTION

1. I have been retained as an expert witness on behalf of Commonwealth Scientific and Industrial Research Organisation (“CSIRO”) for the above-captioned Petition for Post-Grant Review (“PGR”) of U.S. Patent No. 11,260,095 (“the ‘095 Patent”). I am being compensated for my time in connection with this PGR at a consulting rate of \$290 (USD) per hour. My compensation is in no way dependent on the outcome of this matter.

II. QUALIFICATIONS

2. Attached to this Declaration as “**Appendix A**” is my curriculum vitae, which provides a more detailed description of my education, training and experience in the relevant technology. Presently, I am the Director of Synthetic Biology at Napigen, where I study the science of molecular biology. I am also presently an independent biotechnology consultant in industrial and agricultural biotechnology, including genetic engineering of plants and microbes, biofuels, edible oils, and fish oil.

3. I served as a senior visiting scientist during a three-month appointment between November 2017 and January 2018 with Henry Daniell of the University of Pennsylvania School of Dental Medicine (Philadelphia, Pennsylvania USA). In this

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capacity, I assisted towards establishing at the Pennovation Center; an agricultural biotechnology startup company relating to protein production in plants. I also held a five-month consultancy between December 2016 and April 2017 with Zymergen, Inc. (Emeryville, California USA) related to genome engineering.

4. From 1981 to 2016, I was employed with E. I. du Pont de Nemours and Company (“DuPont”). In these 35 years, I held six positions of increasing responsibility in different businesses. While at DuPont between 2002-2012, I played a key role in a project involving the complex metabolic engineering of yeast (59 transgenes) to create perhaps the richest natural source of ω -3 fatty acid, that included the discovery and overexpression of various enzymes known as desaturases, elongases and acyltransferases.

5. While at DuPont between 1986-1994, I also initiated a new area of research and development on the genetic modification of lipids in oil crops. I was among the first scientists to clone genes encoding membrane bound desaturases (Δ -12/ ω -6 desaturases and Δ -15/ ω -3 desaturases) from plants, and I subsequently cloned genes encoding these desaturases from microbes. While my work centered on Δ -15/ ω -3 desaturases, I also became familiar during this time period with the ω -3 desaturase encoded by the *FAT-1* gene of the roundworm *Caenorhabditis elegans*.

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6. I hold a Doctor of Philosophy degree (“Ph.D.”) in Botany/Biochemistry from Michigan State University (East Lansing, Michigan USA). I also earned a Master of Philosophy in Life Sciences from Jawaharlal Nehru University (New Delhi, India), and a Master of Science in Botany from The University of Delhi (Delhi India). I obtained my Bachelor of Science in Botany also from Delhi University.

7. I have published extensively in the field of plant science, including on the topic of uses of ω -3 desaturases. I am the named inventor on at least 65 granted patents as well as on a few pending patent applications, including one filed in August 2018. I have authored over 24 peer-reviewed papers. I received the Invention-Of-The-Year Award in 2008 by DuPont (Pioneer Seed Company) for high oleate soybean, the DuPont Accomplishment Award for novel fatty acid desaturases in 2012, and the DuPont Accomplishment Award in 2013 for generating a yeast strain producing eicosapentaenoic acid at 30% dry cell weight.

III. MATERIALS CONSIDERED

8. I provide opinions in this declaration based on my education, training, background, and experience, as well as the documents I have reviewed to date, including the ‘095 Patent. Those documents, and the other materials cited in this declaration, are listed in **Appendix B**. I have either read the materials listed in **Appendix B** or reviewed summarized data provided by counsel to CSIRO.

IV. LEGAL STANDARDS

9. In preparing this declaration, certain patent law concepts have been explained to me by CSIRO's counsel, including the legal standard for interpreting claims, as well as those for assessing written description, enablement, and anticipation.

A. Written description

10. I have been informed by counsel that a claim in a granted patent must be sufficiently supported by the disclosure in the patent's specification, read in the context of what a person of ordinary skill in the art would have known at the time of the claimed invention. I understand that the basic inquiry for written description is whether the specification provides sufficient information for the person or ordinary skill to recognize that the named inventors possessed the full scope of the claimed invention.

11. I have been informed by counsel that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species of the genus 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. I also understand that 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. I understand that 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.

B. Enablement

12. I have been informed by counsel that, in addition to written description, a patent specification must also enable a person of ordinary skill in the art to make and use the full scope of the claimed invention without undue experimentation as of its effective filing date. I understand that multiple factors should be considered when making this determination. These factors 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.

C. Entitlement of priority

13. I have been informed by counsel that, for the claims of an application to be entitled to an earlier application's filing date, the earlier application must provide written description and enablement of the claims, as of the earlier application's filing date.

D. Anticipation

14. I have been informed by counsel that a claim is anticipated when a single prior art reference discloses, either expressly or inherently, each and every claim element arranged in the order specified by the claim. I also understand that whether a document qualifies as prior art against a claim depends on the effective filing date to which the claim is entitled.

E. Claim Construction

15. I have been informed by counsel that the Patent Trial and Appeal Board ("PTAB") applies the same claim construction standard used in district courts, where the claims are given their ordinary meaning as understood by one skilled in the art at the time of the invention, informed by the claim language itself, the specification, and the prosecution history. I also understand that "extrinsic evidence"—i.e., evidence other than the patent and prosecution history—can be relevant in determining how a skilled artisan would understand terms of art used in the claims.

I have been informed, however, that extrinsic evidence may not be used to contradict the meaning of the claims as described in the intrinsic evidence—i.e., evidence in the claim language itself, the specification, and the prosecution history.

F. Person of Ordinary Skill in the Art

16. In my opinion, 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.

V. SUMMARY OF MY OPINIONS

17. 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 (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.”

18. 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.

19. 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.”

20. I have been asked to consider whether the description in the ‘095 Patent demonstrates that the inventors had possession of the full scope of the invention defined in claims 1-11 of the ‘095 Patent.

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21. I have also been asked to consider whether the POSITA, reading the specification of the '095 Patent, could make and use the full scope of the invention defined in claims 1-11 without undue experimentation, either as of November 14, 2014, or as of November 13, 2015.

22. In my opinion, elaborated below, none of claims 1-11 are adequately described or supported by the '095 Patent. Further, in my opinion, as elaborated below, the specification does not teach the POSITA how to make and use the invention recited in any of claims 1-11 without undue experimentation as of November 14, 2014, or as of November 13, 2015.

23. First, in my opinion, the claims are not supported by a written description because the '095 Patent does not describe a Delta-5 elongase gene under the control of a "FAE promoter."

24. All claims of the '095 Patent require the presence of a Delta-5 elongase gene under the control of a "FAE promoter."¹ However, I noted that the '095 Patent does not include *any mention* of a "FAE promoter," let alone a "Delta-5 elongase

¹ The terms "FAE" or "FAE promoter" are not defined in the '095 Patent. As discussed in section VIII.A, "FAE" could be an abbreviation for "fatty acid elongase."

gene under the control of a purported FAE promoter.” Further, 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. Based on my review of the provisional patent applications, I determined that the genetic constructs used to generate the transgenic plants of the ‘095 Patent employ a Delta-5 elongase isolated from *Ostreococcus tauri* under the control of the promoter from the FAE1.1 gene of *Brassica napus*. I did not see any description in the ‘095 Patent or the provisional applications of a genus or class of “FAE promoter.” Based on this lack of description of a genus or class of “FAE promoter,” it is my opinion that the ‘095 Patent neither describes nor demonstrates possession of a Delta-5 elongase gene under the control of a “FAE promoter” as claimed.

25. Second, in my opinion, 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.

26. Third, I noted that 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 *FAE 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

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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*.”

27. Finally, claims of the ‘095 Patent are anticipated by PCT International Patent Application Publication Nos. WO 2013/185184 and WO 2015/089587 as detailed in this Declaration.

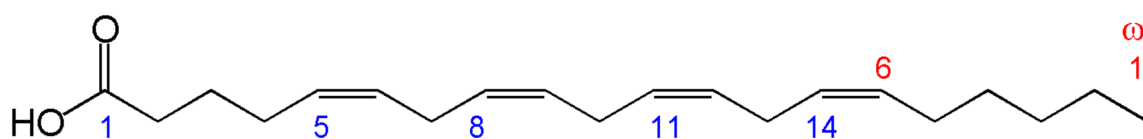
VI. TECHNOLOGY BACKGROUND

28. The '095 Patent relates, generally, to the production of transgenic plants that produce docosahexaenoic acid (DHA), 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.

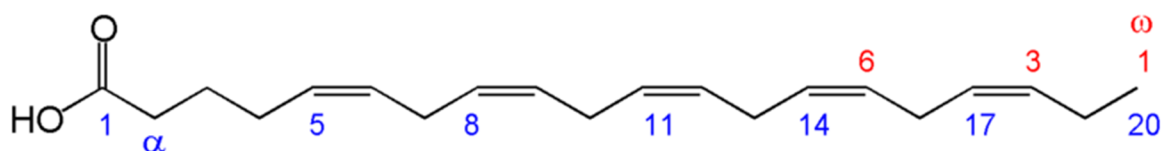
A. Docosahexaenoic Acid (DHA), Eicosapentaenoic Acid (EPA), and Arachidonic Acid (ARA)

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

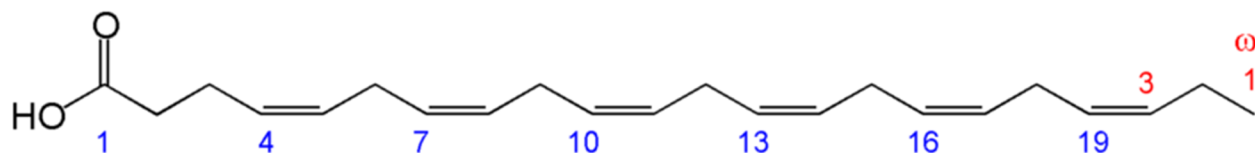
30. The chemical structure of ARA is:



31. The chemical structure of EPA is:



32. The chemical structure of DHA is:



33. 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).

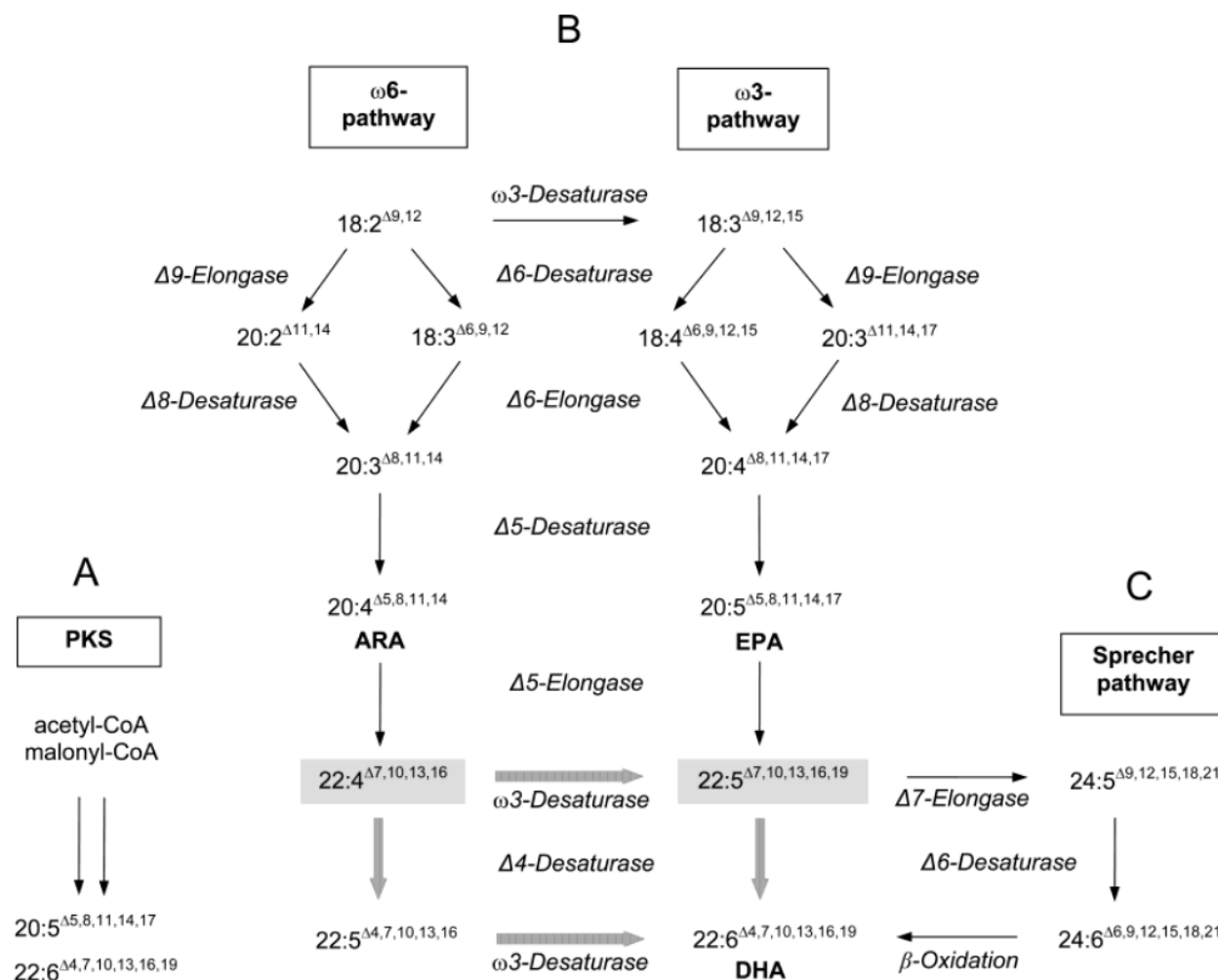
34. When “ ω - x ” notation is used, only the position of the double bond which is closest to the methyl end is indicated, even if multiple double bonds exist and the 20-carbon fatty acid (EPA) shown in the diagram is named “20:5 ω -3” or “20:5n-3.” Accordingly, any PUFA that has its first double bond 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).

35. 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.

B. Biosynthesis of EPA and DHA

36. 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.

37. 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.

1. Elongases

38. 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.² Elongases are often

² 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 -

referred 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).

39. The claims of the ‘095 Patent specifically recite “a Delta 5-elongase gene under the control of a FAE promoter.” According to Figure 1, a Delta 5 ($\Delta 5$)-elongase 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.” A $\Delta 5$ -elongase 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.

2. Desaturases

40. 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

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

the new double bond is created. Other types of desaturase exist, such as ω 3- or 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.

3. Promoters

41. 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.

42. 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 VIII.A, in my opinion 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.

43. 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 *S. chinensis* (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. *FAE1* genes have been found in various *Brassica* species—the species *Brassica rapa* and *Brassica nigra* have one copy of the FAE1 gene, while *Brassica napus* and *Brassica juncea* have two copies (denoted *FAE1.1* and *FAE1.2*).

VII. SUMMARY OF THE ‘095 PATENT

A. The ‘095 Patent

1. The Claims

44. 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.

45. 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.

2. The Specification

46. 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”³ 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.

a. The Delta-5 elongase expression disclosure

47. 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

³ As explained in section VI.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.

that expression of the Delta-5 elongase gene is maintained or increased in late stage seed development.” *Id.* at 7:19-23.

48. 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.

Id. at 7:32-65.

49. 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.

50. I noted that 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, I did not see any disclosure in the ‘095 Patent of a “FAE” promoter, let alone a “Delta-5 elongase under the control of a FAE promoter.”

b. Example 1 of the ‘095 Patent

51. 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.”

52. 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. Ex. 1001, 10:5-44. Example 1 provides the names of the genetic constructs used for each of these transgenic events, explaining 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.” Ex. 1001, 10:5-12. Example 1 further 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.” Ex. 1001, 10:15-19. Further, “[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).” Ex. 1001, 10:19-22. Beyond these explanations, the specification of the ‘095 Patent **does not** provide any further description of the contents of each 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.⁴

c. Example 2 of the ‘095 Patent

53. Example 2 of the ‘095 Patent simply outlines the techniques used to extract and analyze the fatty acid of lipids from seeds collected as described in Example 1. *See* Ex. 1001, 10:19-11:23.

d. Example 3 of the ‘095 Patent

54. 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.

e. Example 4 of the ‘095 Patent

55. 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,

⁴ As explained in section VII.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 an *Ostreococcus tauri* 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.

f. Example 5 of the ‘095 Patent

56. 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.

B. The disclosure of the provisional applications

57. The ‘622 and ‘373 applications are nearly identical, with identical Figures and a nearly identical specification. The ‘373 application appears to contain everything from 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”) as summarized in section VI.B, *supra*.

58. 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.

59. 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.

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

60. As discussed above, the specification of the ‘095 Patent itself 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 specification but are described in the provisional applications. Table 13—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.⁵

⁵ 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

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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.

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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

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

61. 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* 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*.”

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

62. 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%.

63. In the provisional applications I did not see any description of *Brassica napus* plants with these ranges in amounts or ARA, EPA, and DHA.

64. 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 increases.

65. In the provisional applications I did not see any description of harvesting *Brassica napus* plants when the contents of ARA has decreased and did not see any description of *Brassica napus* plants wherein, when grown, the content of ARA decreases or the content of EPA increases.

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

66. As discussed in section VII.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.

67. 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.

C. Examination of the ‘162 application

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

a. Initial filing

68. 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.

69. 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.

Id.

b. March 5, 2020 Office Action

70. 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 as obvious over PCT International

Patent Application Publication No. WO 2013/153404 (“the ‘404 publication”, Ex. 1008.) Ex. 1007, pp. 929-931.⁶

c. September 4, 2020 Amendment

71. 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.

⁶ 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.

72. 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.

d. December 8, 2020 Final Office Action

73. In response to PO’s September 4, 2020 Amendment, the Examiner issued a December 8, 2020 Final Office Action which maintained the obviousness rejection of claims 1-9 and 13-18 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.

e. May 10, 2021 Amendment

74. 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).

f. June 3, 2021 Office Action and allowance

75. 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 presented a new rejection of claims 7 and 13-15 under 35 U.S.C. §103.⁷ 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.

76. During prosecution of the ‘162 application the Examiner never rejected the claims under 35 U.S.C. § 112 for lack of enablement or written description. Similarly, I did not see evidence of the Examiner considering the anticipatory prior art references outlined below.

⁷ I understand that these claims were ultimately cancelled by PO. Therefore, I have not been asked to provide my opinion regarding these claims.

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

77. As discussed in section VII.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.

2. *Brassica napus* plants expressing a Δ 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

78. 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 VII.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 Δ 5-elongase.

79. Further, despite all transgenic events containing a Delta-5 elongase under the control of a *Brassica napus* FAE1.1 promoter (*see* section VII.B.1), only events “LBFLFK” and “LBFGKN” produced seed comprising lipids with levels of EPA, DHA and ARA within the scope of the recited claims, while seeds from events “LANPMZ” and “LAODDN” comprised levels of EPA, DHA and ARA 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.

3. Publications in the art demonstrate that the FAE promoters do not express of the $\Delta 5$ -elongase during late stage seed development

80. 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. 724, left-hand column, second full paragraph.

81. 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.

VIII. DETAILED OPINIONS

A. Claim construction

1. EPA, DHA, and ARA

82. 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 VI.A, *supra*.

83. 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 a 7-100% EPA+DHA. 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, 2-97% DHA, and 0-4% ARA.

2. Delta-5 elongase

84. 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 $\Delta 5$ -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 $\Delta 5$ position as discussed in section VI.B.1, *supra*.

3. FAE promoter

85. The “FAE promoter” is not recited or defined anywhere in the ‘095 Patent. Nevertheless, given its ordinary customary meaning, in my opinion 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 VI.B.3, Promoters of FAE genes have been identified in various species, including *Arabidopsis thaliana*, *Brassica napus*, *Brassica rapa*, *Brassica nigra*, *Brassica juncea*, and *S. chinensis*.

4. Late-stage seed development

86. 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.

B. Lack of entitlement to priority

87. As discussed in section VII.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, in my opinion claims 1-11 are not entitled to priority of either of the provisional applications.

C. Lack of Written Description of the Claims

88. In my opinion a POSITA would conclude, based on the specification of the '095 Patent and the priority applications that the inventors did not have possession of the invention recited in claims 1-11. 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 “FAE promoter.” The material that PO relies on to support recitation of a “FAE promoter” is found solely in the provisional applications, which I have been informed cannot be relied on for written description of the claims. 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 *Brassica napus* FAE1.1 promoter. 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.”

89. 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.

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”

90. 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, I have been informed that 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, it is my understanding that 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 a Delta-5 elongase gene under the control of *any* “FAE promoter.”

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

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

92. 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 $\Delta 5$ -elongase from *Ostreococcus tauri* under the control of the promoter of the “FAE1.1” gene from *Brassica napus*.

93. 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 VII.C.1.e above. I understand that material that is incorporated by reference

from a provisional application cannot be used to provide written description for a claim.

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

94. The term “FAE promoter,” is not recited or defined anywhere in the ‘095 Patent. Nevertheless,, as discussed in section VIII.A, in my opinion 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.

95. As noted in section VII.B.2 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.

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

96. 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%.”

97. In the specification of the ‘095 Patent, much is made of the expression levels of the Delta-5 elongase during late stage seed development. 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.

98. 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. However, *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.

99. Indeed, as discussed in section VII.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.

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”

100. 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.⁸ 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.

101. 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.

102. 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 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.

⁸ Table FA4 shows a difference between EPA and ARA of 1.96% and 3.28% in the last lipids extracts of events LANPMZ and LAODDN, respectively

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

103. As discussed in section VII.A.2, the specification of the ‘095 Patent asserts that a reduction in ARA 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.

104. However, as discussed in section VII.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.

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”

105. 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.

106. 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 5% to 100% more EPA than ARA.

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

107. 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 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.”

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%”*

108. 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.

109. 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.

110. 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%.

111. 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).

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”

112. 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.

113. 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.

114. 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%.

115. 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.

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

116. As discussed in section VII.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 VII.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.

117. 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.”

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%

118. 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.-%.”

119. 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.

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

120. 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.

D. Lack of Enablement of the Claims

121. In my opinion, 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 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.

1. 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

122. 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.

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

123. 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.

124. 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.

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

125. 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 VII.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 VII.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 POSITA could not make and use the full scope of the claimed invention without undue experimentation.

2. 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

126. 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.

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

127. 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. 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.

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

128. 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 VII.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 VII.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. Based on this disclosure, it is clear that a POSITA could not make and use the full scope of the claimed invention without undue experimentation.

3. 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

129. 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%.

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

130. 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%.

131. 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.

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

132. As noted in the specification of the '095 Patent, 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.

133. 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.

134. 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.

4. **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**

135. 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.”

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*

136. 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.

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*

137. As discussed in section VII.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 VII.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.

5. 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”

138. 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.”

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

139. 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.

140. 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.

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

141. 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 VII.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 VII.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 POSITA could not make and use the full scope of the claimed invention without undue experimentation.

6. 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%

142. 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.-%.”

143. 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.

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

144. 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%.

145. Based on this data, it is clear that a POSITA would not be able to practice the 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.

E. Anticipation of the claims

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

146. 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.

a. Disclosure of the WO 2013/185184

147. 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.

b. Claims 1 and 6 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

<u>Claim</u>	<u>Claim element</u>	<u>Disclosure in WO 2013/185184</u>
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 (20:5 ω 3), and DHA (22:6 ω 3). 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% (20:5 ω 3), and 8.5% DHA (22:6 ω 3). 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.
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 FA 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

<u>Claim</u>	<u>Claim element</u>	<u>Disclosure in WO 2013/185184</u>
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% (20:5 ω 3), and 8.5% DHA (22:6 ω 3). 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.

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

148. 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.

149. As discussed in section VII.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. Accordingly, the claims are not entitled to priority to the filing date of the provisional applications. Although 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.

a. Disclosure of the WO 2015/089587

150. 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.

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.

IX. SUPPLEMENTATION

151. I may prepare the documents cited and/or listed herein, or portions of those documents, for use as exhibits at any hearing or oral argument in this

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proceeding. I may further prepare exhibits that summarize portions of my testimony or key terms or concepts presented therein, or other demonstrative exhibits, for use at any hearing or oral argument in this proceeding.

152. I reserve the right to supplement my testimony and this report in response to any judicial determinations, in response to the opinions expressed by BASF's experts in this proceeding, and/or in light of additional evidence or testimony brought forth to my attention after the date of my signature below.

X. CONCLUSION

153. I hereby declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct, and that all statements made of my own knowledge are true and that all statements made on information and belief are believed to be true. I understand that willful false statements may be punishable by fine or imprisonment or both.

Dated: 11.23.22

By: Narendra S. Yadav

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APPENDIX A

NARENDRA YADAV, Ph.D.

Wilmington, DE

302.593.3114

narenyadav6@gmail.com

[linkedin.com/in/narenyadav6biotechinnovator](https://www.linkedin.com/in/narenyadav6biotechinnovator)

KEY SKILLS

- Demonstrated success in biotechnology, including two “once-in-a-lifetime” breakthroughs:
 - Discovered omega 6 desaturase gene that led to the biotech soybean oil Plenish® benefitting farmers (anticipated to be the 4th largest U.S. row crop by 2023), the food industry, and consumers with its zero trans fat oil (“In a Bean, a Boon to Biotech”, New York Times, Nov 15, 2013).
 - Engineered yeast into the richest source of omega-3 fatty acids, described by Nature Biotechnology as a ‘metabolic-engineering tour de force’. Its use in Verlasso™ salmon replaced 75% of the wild-caught fish needed in aquaculture to earn the distinction of “better alternative” by Seafood Watch.
- Inventor on 65 granted patents, 9 pending; Strong experience in intellectual property, reading and writing patents; Expert witness in two lipid biotechnology patent lawsuits (BASF v Nuseed/CSIRO).
- Author on 24 peer-reviewed papers (1 in 2020) including high impact journals, Nature, Nature Biotechnology, P.N.A.S., and Plant Cell; Frequently asked to peer-review manuscripts for journals.
- Successful metabolic engineering of one plant and two microbes from start to finish and all worked!
- Genetically engineered both central and secondary metabolic pathways in plants and microbes.
- Genome editing in plants and microbes as well as in their organelles (mitochondria and chloroplasts).
- First to deploy Crispr gene editing on a diploid industrial yeast: disrupted both alleles of two independent loci in less than a week, which until then took over 6 months.
- Demonstrated expertise in bioinformatics, gene discovery, cutting edge DNA assembly.
- On-boarded a recalcitrant microbe for high throughput, automated microbe engineering using Benchling platform and robots, such as Mantis, Bravo, Guava, Tecan, and Fragment Analyzer.
- Interest in gene therapy, hybrid wheat, and medicinal cannabis alkaloid biosynthetic pathways.

PROFESSIONAL EXPERIENCE

NAPIGEN, Delaware Innovation Space, Wilmington, DE

Director, Synthetic Biology, Mar 2018-present.

Startup first to achieve gene editing in chloroplast and mitochondrion [B.-C. Yoo, **N. S. Yadav**, E.

M. Orozco, H. Sakai (2020) Cas9/gRNA-mediated genome editing of yeast mitochondria

and *Chlamydomonas* chloroplasts. Peer Review PubMed [31934513](#), Jan 6 2020.]

Napigen awarded new grants in 2019 by Breakout Labs, State of Delaware, and Grantham Foundation for organelle gene editing in agriculture (for hybrid wheat), human healthcare (gene therapy), and industrial biotechnology applications.

SYNBIOBETA, San Francisco, CA. **Bio Ambassador**, Advocating Synthetic Biology. Sep.2019-present

UNIVERSITY OF PENNSYLVANIA, Philadelphia, PA

Senior Visiting Scientist, Nov. 2017 – Jan. 2018

- Ultra-high-level protein production in plant plastids for pharmaceutical, industrial, food, and feed uses.
- Setting up an agricultural biotechnology startup on plant protein production at Pennovation Center.

ZYMERGEN, Emeryville, CA

Genome Engineering Consultant/Scientist on a 5-month project, Dec. 2016 – Apr. 2017.

- Successfully on-boarded a microbe for high throughput, automated microbe engineering using Benchling platform and robots, such as Mantis, Bravo, Guava, Tecan, and Fragment Analyzer.

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Narendra S. Yadav, Ph.D.

- Used cutting-edge DNA assembly, including Gibson assembly, with a powerful Laboratory Information Management system (LIMS) to make a library of different native and heterologous promoters.

INDEPENDENT BIOTECHNOLOGY TECHNICAL CONSULTANT/ADVISOR, Wilmington, DE 2017-present.
Advisor on industrial and agricultural biotechnology, industrial synthetic biology, gene editing, Crispr, genetic engineering of plants and microbes, plant nuclear and plastid transformations, bioinformatics, metabolic engineering, biofuels, edible oils, fish oil, aquaculture, and intellectual property. Yeast (*Saccharomyces cerevisiae* and *Yarrowia lipolytica*) nuclear and mitochondria based production of proteins.

SCIENCE, TECHNOLOGY & RESEARCH INSTITUTE OF DELAWARE, Wilmington, DE
Founding Member 2016 –2018.

DUPONT CO., Wilmington, DE. Held 6 positions of increasing responsibility over 35 years in different businesses in both technical and non-technical roles 1981 - 2016.

Senior Principal Investigator, Yeast biofuels 2013 - 2016.

- Met a key business/technical milestone of reducing acid in the medium by 50% by genetic engineering to improve downstream economics of butanol production.
- Improved yield of ethanol by 10% by proposing and successfully testing a new pathway in lab.
- First to develop novel Crispr gene editing tool for engineering a diploid industrial yeast: disrupted both alleles of two independent loci in less than a week, which before took over 6 months.

Senior Research Associate, Fatty acid engineering 2002 - 2012.

- Played key role in a complex (59 transgenes) metabolic engineering of the oleaginous yeast, *Yarrowia lipolytica*, to make it the richest source of omega-3 fatty acid in nature, including discovering and overexpressing different desaturases and acyltransferases.
- This pioneering work made *Yarrowia* a platform of choice for producing hydrocarbons worldwide.

Research Associate, Plant Gene Expression 1994 - 2001.

- Developed proprietary (5 patents) genetic switches for generational control of transgene expression for containing transgenic traits.
- Supervised teams of Research Associates, summer interns, and a post doc.

Senior Research Biologist, Molecular biology of oil biosynthesis 1986 - 1994.

- Initiated a new area of R&D on genetic modification of lipids in oil crops. One of the first to clone plant soluble delta-9 desaturase and $\Delta 12/\Delta 15$ desaturases by T-DNA tagging. Managed IP landscape.
- Key contributor to the cloning of omega 6 desaturase gene that led to trans-free high oleate soybean Plenish® oil to benefit consumers, food industry and farmers (anticipated to become the 4th largest U.S. row crop by 2023).

Technical Analyst, R&D liaison to corporate business development team 1984-1985.

- Identified new business opportunities in agricultural biotech, such as modified vegetable oils. Made presentations to prospective business partners and customers, such as McDonald, Kraft, P&G.
- Demonstrated my ability to influence and sell my strategic vision on healthy vegetable oils by successfully initiating an entirely new R&D program.
- Initiated and oversaw DuPont's R&D contract with DNA Plant Technology that led to Inter Mountain Canola joint venture to commercialize genetically improved canola oil.

Staff Scientist, Plant Molecular Genetics 1981-1984.

- Developed in house agrobacterium plant transformation.
- Co-inventor of sulfonylurea (SU) herbicide resistance gene; commercialized SU herbicide-resistant crops.

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Narendra S. Yadav, Ph.D.

WASHINGTON UNIVERSITY, St. Louis, MO

American Cancer Society Postdoctoral Fellow with Dr. Mary-Dell Chilton, plant transformation pioneer. Provided first evidence for the integration of bacterial DNA in agrobacterium-infected cells that led to the development of agrobacterium transformation vector that is still the key method for making GMO crops.

PATENTS/PAPERS/AWARDS

- Inventor on 63 granted patents (4 on herbicide resistance, 12 on plant genetic engineering, 5 on controlling plant gene expression, and 42 on microbial metabolic engineering), and 9 pending. (List of my patents available on request)
- Author on 24 peer-reviewed research papers in areas of metabolic engineering, gene discovery, and gene expression in high impact journals, such as Nature, Nature Biotechnology, P.N.A.S., and Plant Cell. First author on 5 and senior author on 7. (List of my peer-reviewed publications available on request). Most recent publication:
B.-C. Yoo, **N. S. Yadav**, E. M. Orozco, H. Sakai (2020) Cas9/gRNA-mediated genome editing of yeast mitochondria and *Chlamydomonas* chloroplasts. Peer Review PubMed [31934513](#), Jan 6 2020.
- Invention-Of-The-Year Award by Pioneer Seed Company for high oleate soybean, 2008.
- DuPont Accomplishment Award for novel fatty acid desaturases, 2012.
- DuPont Accomplishment Award for generating yeast strain producing EPA at 30% DCW, 2013.
- BCS&E Catalyst Award for the startup of DuPont Knowledge Center, Hyderabad, India, 2008.

OTHER ACTIVITIES

- Travel to exotic places, such as S. Africa safari, Green Island, Australia
- Movies, especially Alfred Hitchcock movies
- Science writing for SynBioBeta
- Volunteer judge for two years at Delaware Valley Science Fairs

EDUCATION

- **Doctor of Philosophy (PhD) Botany/Biochemistry**
Plant Research Laboratory, Michigan State University, East Lansing, Michigan
- **Master of Philosophy, Life Sciences**
J. Nehru University, New Delhi, India
- **Master of Science, Botany**
Delhi University, Delhi, India
- **Bachelor of Science Honors, Botany**
Delhi University, Delhi, India
- **DuPont Technical Leadership Development Workshop** (2012), a week-long intensive course on business principles and leadership skills.
- **Six Sigma Green Belt Certification**, a 3-month course and application to own research at DuPont
- **Decision and Risk Analysis Course**, a week-long finance course by DuPont.

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APPENDIX B

<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 Δ^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.

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in Support of Petition for Post-Grant Review
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<u>Exhibit No.</u>	<u>Description</u>
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.
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 Arabidopsis thaliana. <i>Plant Molecular Biology</i> , 46(6), 717-725.