**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

| | | |
|---|---|---|
| In re Patent of: | Jeff Addy | |
| U.S. Patent No.: | 11,248,245 | Attorney Docket No.: 47604-0020IP1 |
| Issue Date: | February 15, 2022 | |
| Appl. Serial No.: | 14/578,075 | |
| Filing Date: | December 19, 2014 | |
| Title: | PROCESS AND SYSTEMS FOR CATALYTIC MANUFACTURE OF WAX ESTER DERIVATIVES | |

## DECLARATION OF THOMAS SCHULTZ

I currently hold the opinions set expressed in this declaration. But my analysis may continue, and I may acquire additional information and/or attain supplemental insights that may result in added observations.

I hereby declare 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 further declare that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of the Title 18 of the United States Code.

Dated: 12-6-23 By: Thomas Schultz

Thomas Schultz

## TABLE OF CONTENTS

## LIST OF EXHIBITS

| Exhibit | Description |
|---|---|
| 2001 | Declaration of Dr. Tom Schultz, Ph.D. In Support of Patent Owner's Preliminary Response |
| 2002 | G. Knothe, *Structure indices in FA chemistry. How relevant is the iodine value?* JAOCS, 79 (9) 847-854 (2002). |
| 2003 | Claim Construction Memorandum Opinion (Dkt No. 63) filed in *Cargill, Incorporated v. Vantage Specialty Chemicals, Inc.*, No. 1:22-cv-00979-RGA-SRF (D. Del. June 5, 2023) |
| 2004 | Excerpt of United States District Courts, Federal Court Management Statistics Report for the 12-month period ending March 31, 2023, *available at* https://www.uscourts.gov/sites/default/files/data_tables/fcms_na_distprofile0331.2023.pdf |
| 2005 | Initial Invalidity Contentions (Dkt No. 27) filed in *Cargill, Incorporated v. Vantage Specialty Chemicals, Inc.*, No. 1:22-cv-00979-RGA-SRF (D. Del. Jan. 19, 2023) |
| 2006 | Markman Claim Construction Order (Dkt No. 67) filed in *Cargill, Incorporated v. Vantage Specialty Chemicals, Inc.*, No. 1:22-cv-00979-RGA-SRF (D. Del. June 15, 2023) |
| 2007 | Declaration of Ahmed Davis |
| 2008 | Declaration of Casey Kraning |
| 2009 | Declaration of Dr. Tom Schultz, Ph.D. In Support of Patent Owner's Response |
| 2010 | Sharma et al., "Textbook of Cosmetic Formulations", https://www.researchgate.net/publication/325023106, May, 2018 |
| 2011 | Castillo, et al. "Medium-engineering: a useful tool for modulating lipase activity and selectivity", Biocatalysis 2015, Vol. 1 pp. 178-188 |
| 2012 | CONFIDENTIAL Cargill Certificate of Analysis for Floraesters® 15, February 26, 2004 |

| | |
|---|---|
| 2013 | CONFIDENTIAL Cargill Certificate of Analysis for Floraesters® 20, September 1, 2004 |
| 2014 | CONFIDENTIAL [redacted] |
| 2015 | Grand View Research, Inc. "Personal Care Specialty Ingredients Market Size, Share, & Trends Analysis Report By Product (Active, Inactive), By Application (Skin Care, Hair Care, Oral Care, Color Cosmetics, Others), By Region, And Segment Forecasts, 2023 – 2030", https://www.grandviewresearch.com/industry-analysis/personal-care-specialty-ingredients-market, 2023 |
| 2016 | National Academy of Sciences, "Biobased Industrial Products: Priorities for Research and Commercialization", Committee on Biobased Industrial Products, National Research Council, ISBN: 0-309-52185-8, 2000 |
| 2017 | Covestro, "End-of-Life Myths and Facts about Cosmetic Ingredients" https://solutions.covestro.com/en/highlights/articles/stories/2019/biodegradability-and-cosmetics#:~:text=Only%20natural%20products%20can%20biodegrade,nature%20and%20are%20easily%20biodegradable. 2023 |
| 2018 | Wilford, "Oil From a Shrub Found in Desert May Save the Sperm Whale", The New York Times, https://www.nytimes.com/1975/05/15/archives/oil-from-a-shrub-found-in-desert-may-save-the-sperm-whale.html May 15, 1975 |
| 2019 | LibreTexts, "4.3: Mechanisms of Catalysis", https://batch.libretexts.org/print/Letter/url=https://bio.libretexts.org/Bookshelves/Biochemistry/Book%3A_Biochemistry_Free_For_All_(Ahern_Rajagopal_and_Tan)/04%3A_Catalysis/4.03%3A_Mechanisms_of_Catalysis.pdf |
| 2020 | Saldana, et al. "Oxidative Stability of Fats and Oils Measured by Differential Scanning Calorimetry for Food and Industrial Applications", Applications of Calorimetry in a Wide Context, Chapter 19; pp 445-474, 2013 |

| | |
|---|---|
| 2021 | Gomna , “Review of vegetable oils behaviour at high temperature for solar plants: Stability, properties and current applications,” https://www.sciencedirect.com/science/article/pii/S0927024819302855, 2019 |
| 2022 | RESERVED |
| 2023 | Wen, “Plant protein-derived antioxidant peptides: Isolation, identification, mechanism of action and application in food systems: A review” Trends in Food Science & Technology 105 (2020) pp. 308–322 |
| 2024 | Excerpts, Smith, et al. “March’s Advanced Organic Chemistry” Sixth Edition, Wiley-Interscience, 2007 |
| 2025 | Gad, et al. “Jojoba Oil: An Updated Comprehensive Review on Chemistry, Pharmaceutical Uses, and Toxicity”, Polymers (Basel) 2021 Jun; 13(11): 1711 |
| 2026 | Faller, “UCD Biophysics 241: Membrane Biology“ LibreTexts, https://phys.libretexts.org/Courses/University_of_California_Davis/UCD%3A_Biophysics_241_-_Membrane_Biology October 11, 2023 |
| 2027 | Jadhav, et al. “Triglycerides of medium-chain fatty acids: a concise review,” J Food Sci Technol (August 2023) 60(8):2143–2152 |
| 2028 | Casas-Godoy, et al. “Lipases: An Overview”, Chapter 1, p 3-38; from; Lipases and Phospholipases. Methods in Molecular Biology, vol 861. Humana Press., (2018) |
| 2029 | Sharma, et al. “A Review on Applications of Microbial Lipases” International Journal of Biotech Trends and Technology (IJBTT) - Volume 6 Issue 4– October to December 2016 |
| 2030 | Rozenaal, “lnteresterification of oils and fats”, INFORM, Vol. 3, no. 11, November 1992 |
| 2031 | Schuchardt, et al. “Transesterification of Vegetable Oils: a Review”, J. Braz. Chem. Soc., Vol. 9, No. 1, 199-210, 1998 |

| | |
|---|---|
| 2032 | Arumugam, et al. “Production of biodiesel by enzymatic transesterification of waste sardine oil and evaluation of its engine performance”, Heliyon 3 (2017) e00486, 2017 |
| 2033 | Dias Ribeiro, et al. “Production and Use of Lipases in Bioenergy: A Review from the Feedstocks to Biodiesel Production”, SAGE-Hindawi Access to Research, Enzyme Research, Volume 2011, Article ID 615803, 16 pages |
| 2034 | RESERVED |
| 2035 | Rauwerdink, et al. “How the Same Core Catalytic Machinery Catalyzes 17 Different Reactions: the Serine-Histidine-Aspartate Catalytic Triad of α/β-Hydrolase Fold Enzymes”, ACS Catal. 2015, 5, 6153−6176 |
| 2036 | Utama, et al. “Lipase-Catalyzed Interesterification for the Synthesis of Medium-Long-Medium (MLM) Structured Lipids - A Review”, Food Technology and Biotechnology, July-September 2019 \| Vol. 57 \| No. 3 pp. 305-318 |
| 2037 | Lewis, et al. “Biochemistry, Proteins Enzymes”, https://www.ncbi.nlm.nih.gov/books/NBK554481/?report=printable April 24, 2023, 4 pages |
| 2038 | Stergiou, et al. “Advances in lipase-catalyzed esterification reactions”, Biotechnology Advances 31 (2013) 1846–1859 |
| 2039 | Houde, et al. “Lipases and Their Industrial Applications”, Applied Biochemistry and Biotechnology, Vol. 118, 2004 pp. 155-170 |
| 2040 | Berglund, “Controlling lipase enantioselectivity for organic synthesis”, Biomolecular Engineering, Vol.18 (2001) 13–22 |
| 2041 | Bornscheuer, “Methods to increase enantioselectivity of lipases and esterases”, Chemical biotechnology 2002 pp. 543-547 |
| 2042 | Tabee, et al. “Effects of a-Tocopherol on Oxidative Stability and Phytosterol Oxidation During Heating in Some Regular and High-Oleic Vegetable Oils”, J Am Oil Chem Soc (2008) 85:857–867 |

| | |
|---|---|
| 2043 | Khan, et al. "Current developments in esterification reaction: A review on process and Parameters" Journal of Industrial and Engineering Chemistry 103 (2021) 80–101 |
| 2044 | Steinke, et al. "Lipase-Catalyzed Alcoholysis of Crambe Oil and Camelina Oil for the Preparation of Long-Chain Esters", JAOCS 77, 361–366 (April 2000) |
| 2045 | Gunawan, et al. "Lipase-Catalyzed Synthesis of Palm-Based Wax Esters", J. Oleo Sci., Vol. 53, No. 10, 471-477 (2004) |
| 2046 | Deposition Transcript of David Rockstraw, *Vantage Special Chemicals, Inc. v. Cargill, Inc*. PTAB Proceeding No. IPR2023-00589, November 17, 2023 |
| 2047 | Errata sheets, Deposition Transcript of David Rockstraw, *Vantage Special Chemicals, Inc. v. Cargill, Inc*. PTAB Proceeding No. IPR2023-00589, November 17, 2023 |
| 2048 | Arquette, "Effects of Additives on the Oxidative Stability of Botanical Emollients", International Flora Technologies, Ltd., SCC Ontario Chapter – Education Day September 10, 1998 |
| 2049 | Declaration of Delrika Curry |
| 2050 | CONFIDENTIAL [redacted] |
| 2051 | CONFIDENTIAL [redacted] |
| 2052 | CONFIDENTIAL [redacted] |
| 2053 | CONFIDENTIAL [redacted] |
| 2054 | CONFIDENTIAL [redacted] |

| | |
|---|---|
| 2055 | CONFIDENTIAL [redacted] |
| 2056 | U.S. Patent App. Pub. 2016/0177350A1 to Addy, et al. |
| 2057 | CONFIDENTIAL [redacted] |
| 2058 | LibreTexts, "26.8: Triglycerides", https://chem.libretexts.org/Bookshelves/Introductory_Chemistry/Introductory_Chemistry_(CK-12)/26%3A_Biochemistry/26.08%3A_Triglycerides (last accessed Dec. 5, 2023) |
| 2059 | Biochemistry Free For All, Version 1.3, Oregon State University, Section 4.3: Mechanisms of Catalysis |
| 2060 | FDA, "Are All 'Personal Care Products' Regulated as Cosmetics?" https://www.fda.gov/industry/fda-basics-industry/are-all-personal-care-products-regulated-cosmetics June 16, 2022 |
| 2061 | Carli, "Cosmetic Formulations: A Beginners Guide", Institute Of Personal Care Science; 2020 |
| 2062 | Karupaiah, et al. "Effects of stereospecific positioning of fatty acids in triacylglycerol structures in native and randomized fats: a review of their nutritional implications", Nutrition & Metabolism 2007, 4:16 |
| 2063 | Pleiss, et al. "Anatomy of lipase binding sites: the scissile fatty acid binding site", Chemistry and Physics of Lipids, 93 (1998) 67–80 |
| 2064 | Salvi, "Chapter 4, Transesterification methods", Production of Biodiesel from Non-Edible Sources, 2022, p. 117-151 |

I, THOMAS SCHULTZ, hereby declare the following:

## I. QUALIFICATIONS AND BACKGROUND INFORMATION

1. My education and experience are described more fully in the attached curriculum vitae (APPENDIX A). For ease of reference, I have highlighted certain information below.

2. I received my B.A. in Russian Languages/Chemistry-Physics Minor in 1977, my M. Sc. (Chemistry) in 1979, and my Ph.D. in Physical-Organic Chemistry in 1985 all from New York University. My Ph.D. research was funded under an NHI Cancer Research Grant (1977-1981) to myself and Professor G. Underwood of New York University and which included a term at the Naylor Institute For Cancer Research in Westchester, New York. I attended INSEAD, Fontainebleau, France in 1996 for Business Management.

3. I currently consult in the fields of chemistry and chemical materials used in the personal care and over-the-counter products with a focus on product development including intellectual property, formulations, and product safety.

4. My scientific expertise crosses product formulation, new materials development, and hair and skin science. I have extensive experience in the practice of product development, U.S. and international product safety criteria, including human safety testing, product scale-up from bench top to commercialization, consumer product research, and product packaging stability testing and the

international regulations for package labeling. I began work at Clairol, Inc. (Stamford, CT) as a bench chemist being trained in the processes required to develop formulations for hair care including hair coloring, bleaching, shampooing and conditioning and styling, all practices that use oils and waxes in their product compositions. These practices included the evaluation of those chemicals used in personal care products for their efficacious qualities in their ability to form creams and oil-water emulsions. Optimization of the choice of such oils and waxes involved iterative formula development based on both laboratory bench testing and the inputs of professional cosmetologists' evaluations to modify the formulations per the sensorial information they provided. Performing the initial product stability assessments protocols was needed in order to preview any potential failures of the formulation early in the development process. For example, hair coloring products require an essentially air-free formulation to protect the latent hair dye materials. Product safety protocols were also part of this process including at that time, animal safety studies (e.g., the Draize test on rabbit eyes to predict skin irritation, later replaced with non-animal models such Sintext, etc.) and human safety testing (e.g. the Human Repeat Insult Patch Test, HRIPT) on volunteers and a test for resistance of any microbial growth. These practices are those that have been developed over decades of personal care products testing, and rigorously followed for products such

as hair dyes and bleaches which have the most potential to cause irritation on human skin and scalp so that certain materials are often used based on their safe history.

5. During my career at Clairol I was promoted through to Group Manager, supervising a team of 5 to10 chemists and laboratory technicians, in hair color and hair care product development, basic hair science research, and novel materials' development (hair dyes, hair conditioning materials, hair bleaching compositions). During this time I established contract research programs on hair science with The Textile Research Institute (Princeton, NJ) on hair structure and the effects of chemicals thereupon, Yale University (with Dr. J. Pawlek) and The University Of Naples (Prof. G. Prota) and the Medical University of Silesia, Poland (Prof. T. Sarna). This experience of forward searching research on hair enabled new materials development as a model for building a cadre of performance enhancing materials on call for marketing needs. Clairol, as a fast moving consumer goods company with much competition in their respective markets, necessitated performing new product development based on searching for or developing technologies that would solve for unmet performance needs as defined by the consumer. This involved the exploration of various materials or compositions of matter concurrently and systematically setting up many simultaneous formulations and performing the on bench testing and moving the best performing items into the testing salon. Through this work I became

very familiar with many chemical suppliers gaining knowledge of the classes of chemicals, e.g., surfactants, waxes, oils and others.

6. I have several patents from my time at Clairol and made numerous presentations at cosmetic chemists and science meetings. My experience at Shiseido Ltd.'s ZOTOS division began as a Group Manager rising to Vice President of Research and Development and for one year concurrently as Vice President of Manufacturing. I was responsible for all aspects of product development, including formulation development, basic hair science research, formula globalization (the modification of formulations for use at any of Shiseido's global markets), intellectual property oversight for formulations. Formula globalization required the in-depth knowledge of the materials used in the products such that an intimacy with many chemical suppliers to the trade was established. In this activity the coordination of materials and parts for product manufacture on the 100,000 pcs and higher scale is not trivial. Materials, especially what are known as the commodity chemicals such as waxes, oils, emulsifiers and similar, were needed in large supply so that those chemicals selected for use in the products were often proprietary, covered by a patent or otherwise unique.

7. My experience at L'Oreal's USA company, COSMAIR, included product research and development for hair color, hair bleaching, hair care and hair styling for its professional hair care products in the U.S. initially branching to global

brands. My responsibilities included formulation development, product safety, microbial challenge, stability testing, claims development including testing and documentation, patent review and inventions development, competitive products analysis and evaluations, test salon supervision, harmonization of the various brands' formulations to meet L'Oreal's global materials-use compliance, external materials and hair science programs and oversight of the scale-up laboratory for the New Jersey facility. I also served as hair color product development liaison between the U.S. R&D and France Clichy Hair Color R&D teams. During this time, I was also responsible for innovations including those for skin care and makeup. Additionally I served as one of the liaisons to the corporate headquarters in France for intellectually property development.

8. My experience at P&G as Director of Skin Care included the development of new skin care technology and the development of 'on-demand' skin care products manufacturing for P&G's reflect.com internet business. This included all aspects of skin care product development (formulations, safety and quality assurance/ quality control parameters, claims development and proofs, usage directions) and small scale manufacturing at their KOLMAR-Port Jervis, NY facility. My work experience at E. I. DuPont de Nemours (Wilmington, DE), President, aspect llc Division, was as materials and innovations lead market developer. In this role we successfully identified and placed both technologies and

materials on hand at DuPont to specific unmet performance needs in the personal care product space. My experience at NuSkin Inc. (Provo, UT) was initially as a consultant then as an interim executive for all of their product development, manufacturing (all products provided as finished by 3rd party suppliers), quality assurance and quality control, regulatory compliance, and supply chain needs globally. NuSkin distributes products into more than 50 countries.

9. My experience at Playtex Products, Inc. as Senior Vice President, Chief Technology Officer included all product development (sun-care, infant care, feminine care and personal care products) and their needed claims development and product testing and documentation, regulatory affairs, intellectual property development, safety and Quality Assurance and Quality Control, product scale up, and Consumer Affairs-Complaints.

10. My experience with Baker Street Laboratories LLC was as a consultant to F500 and smaller companies was in the areas of market opportunities, materials development and placement, strategy, claims development, M&A, legal reviews, and litigation support.

11. My experience at Horizon Partners Ventures LLC was as co-founder; a business helping monetize early stage inventions and innovations throughout licensing or technology sale.

12. My experience with litigation, including my work as an expert and testimony that I have provided is listed below:

- Shiseido Ltd.; Defendant (1990) - Personal injury; Dayton, Ohio. Deposition and testimony; Settled prior to trial completion.
- ZOTOS, Inc. (Defendant) (1994) - Patent Infringement; Darien, CT; Deposition; Settled prior to trial.
- Playtex Products, Plaintiff (2007) v. P&G Inc - Product Claims; Westport, CT; Deposition; Settled prior to trial.
- Playtex Products, Defendant (2007) vs. Hatfield - Personal injury; Allendale, NJ; Deposition; Settled prior to trial.
- CRODA Company; Defendant, v. KOBO Products (2011) - Patent Infringement, Subject Matter Expert; (2017) Expert Report and Deposition; Settled 2018.
- CRODA Company; Defendant, v. KOBO Products (2015-16) - Patent Infringement, Subject Matter Expert; (2016) Expert Report and Depositions; Settled 2017.
- Olaplex v. L'Oreal; Defendant (2019); Subject Matter Expert (Patent Infringement & *Inter Pares Review);* Depositions.
- Melaluca v. Shaklee, Inc. (2021): Intellectual Property Infringement *Inter Partes Review* work.
- Combe Incorporated; U.S. complaint of injury; depositions. (2022)

13. I have provided expert consultation for numerous companies since 2002 on product development for hair and skin care products for retail and doctor distribution pathways, new materials development for specialty chemical companies, and several 'private label' personal care product companies. My experience with the chemicals and materials used in formulations of personal care

and medicinal products including my work as a consultant with materials selection and formulation development that I have provided is listed below:

- **2002: E. I. DuPont**, Technology repurposing; IP re-utilization.
- **2003- NuSkin Ltd.,** Dermatology based skin care; Sun Protection skin care, makeup globally; Nutritional Supplements. Litigation Support.
- **2009: International Flavors and Fragrances (IFF), Inc.**, General advisement; strategic planning for new initiatives (food & beverage technologies).
- **2009: CRODA PLC.,** Patent Infringement; raw materials strategy.
- **2009-2010: Shaklee Products**, Skin Care/ Sun care; Materials, Formulations and regulatory compliance; Consumer Safety project management: Litigation support.
- **2010-2011: Symrise GmbH,** Skin Care ingredients (organic) and new materials.
- **2011-2012: CRODA, PLC**, Patent Infringement; raw materials strategy.
- **2014-2016: Dermatologist Skin Care Brands, various luxury brands,** New Product Planning and Procurement- Skin Care/ Sun care;

Materials, Formulations and regulatory compliance; Consumer Safety project management.

- **2017- 2019: Presperse Inc.,** Skin Care/ Sun care; Materials, Formulations and regulatory compliance.

14. I have made in excess of forty presentations to industry and academic and professional organizations during my career. In addition, I have approximately sixty U.S. and International patents and patent applications filed predominantly during work with the corporations I was employed with. These are provided in the Addendum along with my publications list. Being an employee of corporations limited publishing in open journals due to trade secret concerns.

15. I have been the recipient of several awards beginning with a National Institutes of Health Grant Award (1978-80); and within the industries I was employed including The Society Of Cosmetic Chemists Annual Science Award; P&G Research Fellow Award; The Greater Philadelphia Executive Group Annual Award; and have served on the following Boards of Directors positions:

- **American Chemical Society**, Retired General Member;
- **Product Development & Manufacturers Association**, Past General Member;
- **Society Of Gynecological Research**, Past Executive Board Member, expired;

- **Executive Research Council**, Technology Executive Committee, consulting member;
- **Personal Care Products Council**, Scientific Advisory Council-consulting member;
- **Past Board of Directors, *The DaVinci Schools***, Los Angeles County Charter School Initiative; retired; and
- **Past Board of Advisors- QED Program, *The City University Science Center,*** Philadelphia, PA; as needed.

16. I have been retained on behalf of Cargill, Inc. ("Cargill") to offer technical opinions related to U.S. Patent No. 11,248,245 ("the '245 patent") (EX 1001) and prior art references relating to its subject matter. I have reviewed the '245 patent. In addition to any materials cited in the present declaration, I have also reviewed the following references:

- Ex. 1004: Melanie Cummings et al., *A natural alternative*, SOAP, PERFUMERY AND COSMETICS (SPC) ASIA (May 1, 1999) ("Cummings");
- Ex. 1005: James Brown & Robert Kleinman, Trans *Isomers in Cosmetics*, SOAP & COSMETICS at 33 (May 2001) ("*Trans* Isomers 1");

- Ex. 1006: James Brown & Robert Kleinman, Trans *Isomers in Cosmetics Part 2*, SOAP & COSMETICS at 44 (June 2001) ("*Trans* Isomers 2");
- Ex. 1007: U.S. Patent No. RE38,141E1 to Brown et al. ("Brown");
- Ex. 1008: Xuebing Xu, Engineering of enzymatic reactions and reactors for lipid modification and synthesis, 105 EUR. J. LIPID SCI TECH. 289 (2003) ("Xu");
- Ex. 1009: David J. Sessa, Derivation of a Cocoa Butter Equivalent from Jojoba Transesterified Ester via a Differential Scanning Calorimetry Index, 72 J. SCI. FOOD AGRI. 295 (1996) ("Sessa").

17. I have also reviewed various supporting references and other documentation as further noted in my opinions below.

18. Counsel has informed me that I should consider these materials through the lens of one of ordinary skill in the art related to the '245 patent at the time of the earliest possible priority date of the '245 patent, and I have done so during my review of these materials. The '245 patent was filed December 19, 2014 ("the Critical Date"). Counsel has informed me that the Critical Date represents the earliest possible priority date to which the challenged claims of '245 patent are entitled, and I have therefore used that Critical Date in my analysis below.

19. I have no financial interest in the parties or in the outcome of this proceeding. I am being compensated for my work as an expert on an hourly basis. My compensation is not dependent on the outcome of these proceedings or the content of my opinions.

20. In writing this declaration, I have considered the following: my own knowledge and experience, including my work experience in the fields of chemistry, biochemistry, product formulation, specialty chemicals in the cosmetics, personal care and pharmaceutical products development and intellectual property categories in these areas; my experience in teaching those subjects; and my experience in working with others involved in those fields. In addition, I have analyzed various publications and materials, in addition to other materials I cite in my declaration.

21. My opinions, as explained below, are based on my education, experience, and expertise in the fields relating to the ’245 patent. Unless otherwise stated, my testimony below refers to the knowledge of one of ordinary skill in the art as of the Critical Date, or before. Any figures that appear within this document have been prepared with the assistance of Counsel and reflect my understanding of the ’245 patent and the prior art discussed below.

## II. LEGAL STANDARDS

### A. Terminology

22. I have been informed by Counsel and understand that the best indicator of claim meaning is its usage in the context of the patent specification as understood by one of ordinary skill. I further understand that the words of the claims should be given their plain meaning unless that meaning is inconsistent with the patent specification or the patent's history of examination before the Patent Office. Counsel has also informed me, and I understand that, the words of the claims should be interpreted as they would have been interpreted by one of ordinary skill at the time of the invention was made (not today). Because I do not know at what date the invention as claimed was made, I have used the earliest possible priority date of the '245 patent as the point in time for claim interpretation purposes (the Critical Date).

### B. Legal Standards for Obviousness

23. I have been informed by Counsel and understand that documents and materials that qualify as prior art can render a patent claim unpatentable as obvious. I have been informed by Counsel and understand that all prior art references are to be looked at from the viewpoint of a person of ordinary skill in the art at the time of the invention, and that this viewpoint prevents one from using his or her own insight or hindsight in deciding whether a claim is obvious.

24. I have been informed by Counsel and understand that a claim is unpatentable for obviousness under 35 U.S.C. § 103 "if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains." I have been informed by Counsel and understand that obviousness may be based upon a combination of references. I have been informed by Counsel and understand that the combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results. However, I have been informed by Counsel and understand that a patent claim composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.

25. I have been informed by Counsel and understand that when a patented invention is a combination of known elements, a court must determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue by considering the teachings of prior art references, the effects of demands known to people working in the field or present in the marketplace, and the background knowledge possessed by a person having ordinary skill in the art.

26. I have been informed by Counsel and understand that a patent claim composed of several limitations is not proved obvious merely by demonstrating that

each of its limitations was independently known in the prior art. I have been informed by counsel for the Patent Owner and understand that identifying a reason those elements would be combined can be important because inventions in many instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known. I have been informed by Counsel and understand that it is improper to use hindsight in an obviousness analysis, and that a patent's claims should not be used as a "roadmap."

27. I have been informed by Counsel and understand that an obviousness inquiry requires consideration of the following factors: (1) the scope and content of the prior art; (2) the differences between the claims and the prior art; (3) the level of ordinary skill in the pertinent art; and (4) any objective indicia of non-obviousness, such as commercial success, long-felt but unresolved need, failure of others, industry recognition, copying, and unexpected results. I understand that the foregoing factors are sometimes referred to as the "Graham factors."

28. I have been informed by Counsel and understand that an obviousness evaluation can be based on a combination of multiple prior art references. I understand that the prior art references themselves may provide a suggestion, motivation, or reason to combine, but that the nexus linking two or more prior art references is sometimes simple common sense. I have been informed by Counsel

and understand that obviousness analysis recognizes that market demand, rather than scientific literature, often drives innovation, and that a motivation to combine references may be supplied by the direction of the marketplace.

29. I have been informed by Counsel and understand that if a technique has been used to improve one device, and a person of ordinary skill at the time of invention would have recognized that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill.

30. I have been informed by Counsel and understand that practical and common sense considerations should guide a proper obviousness analysis, because familiar items may have obvious uses beyond their primary purposes. I have been informed by Counsel and understand that a person of ordinary skill looking to overcome a problem will often be able to fit together the teachings of multiple prior art references. I have been informed by Counsel and understand that obviousness analysis therefore takes into account the inferences and creative steps that a person of ordinary skill would have employed at the time of invention.

31. I have been informed by Counsel and understand that a proper obviousness analysis focuses on what was known or obvious to a person of ordinary skill at the time of invention, not just the patentee. Accordingly, I understand that any need or problem known in the field of endeavor at the time of invention and

addressed by the patent can provide a reason for combining the elements in the manner claimed.

32. I have been informed by Counsel and understand that a claim can be obvious in light of a single reference, without the need to combine references, if the elements of the claim that are not found explicitly or inherently in the reference can be supplied by the common sense of one of skill in the art.

33. I have been informed by Counsel and understand that secondary indicia of non-obviousness may include (1) a long felt but unmet need in the prior art that was satisfied by the invention of the patent; (2) commercial success of processes covered by the patent; (3) unexpected results achieved by the invention; (4) praise of the invention by others skilled in the art; (5) taking of licenses under the patent by others; (6) deliberate copying of the invention; (7) failure of others to find a solution to the long felt need; and (8) skepticism by experts. I understand that evidence of secondary indicia of non-obviousness, if available, should be considered as part of the obviousness analysis.

34. I have been informed by Counsel and understand that there must be a relationship between any such secondary considerations and the invention, and that contemporaneous and independent invention by others is a secondary consideration supporting an obviousness determination.

35. In sum, my understanding is that prior art teachings are properly combined where one of ordinary skill having the understanding and knowledge reflected in the prior art and motivated by the general problem facing the inventor, would have been led to make the combination of elements recited in the claims. Under this analysis, the prior art references themselves, or any need or problem known in the field of endeavor at the time of the invention, can provide a reason for combining the elements of multiple prior art references in the claimed manner.

36. I have been informed by Counsel and understand that in an *inter partes* review, "the petitioner shall have the burden of proving a proposition of unpatentability," including a proposition of obviousness, "by a preponderance of the evidence." 35 U.S.C. §316(e).

## III. OVERVIEW OF CONCLUSIONS FORMED

37. This declaration explains the conclusions that I have formed based on my analysis. To summarize those conclusions, based on my knowledge and experience and my review of the prior art publications listed in this document, I believe that:

38. The prior art references relied on in Grounds 1-4 do not render obvious the claimed invention in at least because none of the references teach or suggest the use of a lipase to catalyze an ester-ester exchange in jojoba wax esters, and a person of ordinary skill in the art would not have understood that lipases, which to date had

only ever been used to transesterify triglycerides, could work on jojoba wax esters, given the unique structural differences between jojoba wax esters and triglycerides.

39. Further, a person of ordinary skill in the art would not have understood that lipases could be used with jojoba wax esters to generate improved, beneficial properties including increased oxidative stability, lower viscosity, and improved appearance, as compared to the properties attained using a chemical catalyst.

40. In my opinion, a POSITA as of the Critical Date would not have been motivated to combine the references in Grounds 1-4 as Vantage contends, and further would have had no reasonable expectation of success in achieving the claimed invention of the ’245 patent. Thus, Vantage’s Petition has not shown that the claimed invention is unpatentable based on the combinations of references presented in Grounds 1-4.

## IV. LEVEL OF ORDINARY SKILL IN THE ART

41. In my opinion, a person of ordinary skill in the art as of the Critical Date of the ’245 patent (hereinafter a “POSITA”) would have had at least a B.S. in Chemical Engineering, Chemistry, or a related field, and three years of work experiences working in the specialty chemicals industry, although more education or skill might make up for less experience and vice-versa.

42. Based on my experiences, I have a good understanding of the capabilities of one of ordinary skill. Indeed, I have participated in organizations and

worked closely with many such persons over the course of my career. Based on my knowledge, skill, and experience, I have an understanding of the capabilities of one of ordinary skill. For example, from my industry experience, I am familiar with what an engineer would have known and found predictable in the art. From my industry experience, I also have an understanding of the knowledge that a person with this academic experience possesses. Furthermore, I possess those capabilities myself.

## V. TECHNOLOGY OVERVIEW

### A. Personal Care Products

43. Personal care products encompass a wide range of goods designed for individual grooming, hygiene, beautification, self-care and overall enhancement of personal appearance and well-being. Personal care products include various products intended for skincare, haircare, oral care, cosmetics, fragrances, bath and shower items, and other toiletries. Ex. 2060, 1; Ex. 2061, 6–8; Ex. 2010, 5–6; Ex. 2015, 1–2. Manufacturers, producers, and retailers within the personal care products industry create and distribute an extensive array of items, ranging from basic everyday necessities like soaps and shampoos to specialized skincare treatments, makeup, and perfumes. The industry focuses on developing formulations, products, and innovations that cater to diverse consumer needs, preferences, and evolving trends in beauty, health, and self-care. Ex. 2061, 1.

44. In the personal care products industry, oils have historically been used to formulate products with desirable cosmetic and functional properties. With the rise of mass production of personal care products in the 20th century, petroleum-based oil derivatives such as petroleum jelly became prominent due to their high stability and low cost, leading to the formulation of many skincare and haircare products. *Id*. 59-60; Ex. 2016, 16. Over the past several decades, however, the personal care products industry has shifted away from petroleum-based products toward naturally-derived alternatives that have fewer health and safety concerns, as well as less of an environmental impact. Ex. 2016, 16–17. Petroleum-based products are non-renewable and their extraction and production often involve processes that contribute to environmental degradation. Naturally-derived ingredients, on the other hand, are sourced from plants or other renewable resources, and are generally more sustainable and eco-friendly. Ex. 2061, 61. Naturally-derived ingredients can also be more biodegradable, which while desirable from a waste perspective, can be a challenge in terms of stability. Ex. 2017, 2.

45. Unlike many food products that are designed to be consumed relatively quickly, cosmetics and personal care products may sit in drawers and medicine cabinets for months, or even years. Stability is therefore a key performance parameter for any material used in these applications. Ex. 2061, 32; Ex. 2020, 447. For oils used in personal care products, specific aspects of stability can include

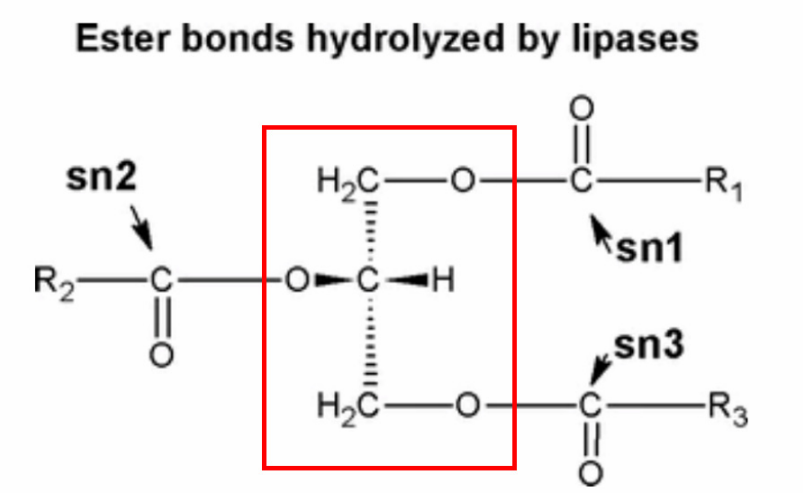
oxidative stability, physical stability, and temperature stability. Oxidative stability refers to an oil's resistance to oxidation, i.e., reaction with oxygen, which can cause rancidity, discoloration, and breakdown of beneficial properties. Ex. 2061, 10. Addition of antioxidants can be used to prevent or slow down oxidation. *Id*., 4. Physical stability means that the oil will not separate or undergo phase changes, maintaining a consistent texture and appearance over the shelf life of the product. Emulsifiers or stabilizers can be used to maintain physical stability. *Id*., 9. Temperature stability means the ability of the oil or product to withstand a range of temperatures without altering its properties significantly. Ex. 2021, 2.

46. Natural oils are generally less oxidatively stable than petroleum-based oils or products. For example, while petroleum jelly can be viable for over a decade, vegetable oil may only last a couple of months and fish oil only a couple of hours. While natural oils can be supplemented with antioxidants to improve oxidative stability, antioxidants are expensive, and therefore incorporating them into a formulation can significantly increase the associated manufacturing costs. Ex. 2023, Abstract. A desire thus exists for natural oils that have greater oxidative stability, thereby requiring the use of fewer antioxidants and further extending the shelf-life of finished products.

### B. Chemical Structure of Naturally Derived Oils and Jojoba Wax Esters

47. Because most of the prior art references relied on in the grounds deal with the transesterification of triglycerides, I provide a brief overview here of the relevant components of a triglyceride. It should be noted that almost all naturally derived oils are made of triglycerides.

48. Triglycerides, also referred to as triacylglycerols, are tri-esters consisting of a glycerol backbone linked to three fatty acids via ester bonds, as shown in the chemical structure below. The glycerol backbone is identified in the red box. The three fatty acids attached to the glycerol backbone can be identical or different, The positions of the fatty acids along the glycerol backbone are indicated using the following "*s*tereospecific *n*umbering": *sn*-1, *sn*-2, and *sn*-3. Ex. 2062, 1.




**Triglyceride structure.**

49. The carbon chain length of the fatty acids, number and position of double bonds with the fatty acids, and the position of fatty acids in the triglyceride molecules are each very important factors affecting physicochemical, functional and nutritional properties of the oil. Ex. 2036, 1. In most triglycerides, the fatty acid chains can have between sixteen and eighteen carbons each.

50. It is well understood that jojoba wax esters are unique among seed oils (i.e., oils derived from the seeds of plants), in part because they do not share the triglyceride structure of other oils. *See* Ex. 1004, 1 (noting that in contrast to jojoba wax esters, "all other seed oils are triglycerides"). Jojoba wax esters are derived from the jojoba plant, traditionally grown in deserts in North America, which produces a "unique seed and oil utilising very little water and the paucity of nutrients found in the soil of its native habitat." *Id*. The jojoba plant "efficiently convert[s] these nutrients and abundant sunshine into a versatile oil with exceptional stability and a purity of composition not duplicated by either man or nature." *Id*.

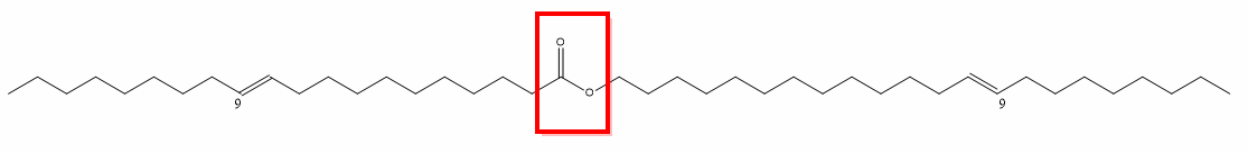
51. While jojoba wax esters have been used for centuries by Native Americans, they were not used commercially until the 1970's, when the personal care industry sought a replacement for sperm whale oil in response to international treaties outlawing the hunting of sperm whales. Ex. 2024, 2-3. Jojoba oil was "touted as being similar in composition to sperm whale oil" but "superior in most applications," because unlike sperm whale oil, "jojoba oil has no fishy odour and no

undesirable triglycerides." Ex. 1004, 1; *see also* Ex. 2025, 1-2. Further, jojoba wax esters were also "the only unsaturated liquid wax readily extractable in large quantities from plant sources." Ex. 2025, 1. Jojoba wax esters are considered beneficial because it is "oxidatively stable, plant-derived, oil-free emollients shown to be non-toxic, non-comedogenic, hypo-allergenic and biodegradable." Ex. 1004, 1. Further, jojoba wax esters have the "capability to improve cosmetic, functional and structural properties of a broad array of personal care products." *Id*.

52. I note that from a chemical structure perspective, jojoba wax esters are not technically oils at all, but are instead composed of almost 98% pure waxes, primarily wax esters, with the other 2% containing sterols and vitamins. Ex. 2025, 3-4; *see also* Ex. 1004, 1. ("the jojoba plant bears a peanut sized, dark chestnut coloured seed containing a unique oil that is chemically a liquid wax ester"). Jojoba oil is composed of wax esters of straight-chain acids and alcohols with high molecular weights. *See* Ex. 1028, 5-6.

53. Specifically, jojoba wax esters are monoesters (i.e., having one ester group) with two long carbon chains on either side of the ester: Jojoba wax esters are mainly composed of combinations of C20 and C22 unsaturated fatty acids and alcohols, but can also contain other chains between 16 and 24 carbons. *Id.*; *see also id.*, 7 ("Jojoba esters are proper waxes, with no triglyceride components" and are formed as mixtures of long chain fatty acids and fatty alcohols joined by an ester

bond (together C34 to C46)); Ex. 2025, Table 1. As illustrated below, jojoba wax esters have two double bonds between the ninth and tenth carbons (referred to as the C9 position) on both the alcohol and acid sides, which are separated by an ester bond, shown in the red box. Ex. 1010, 2:51-54 ("A single double bond is located towards the middle of the respective fatty alcohol chain, specifically in the n-9 position (i.e., counted from the terminal (—$CH_3$) group).").




**Jojoba Wax Ester Structure.**

One chain of the ester is derived from a fatty acid, while the other is derived from a fatty alcohol. These chains are much longer than the fatty acid chains in most common triglycerides. Additionally, in my opinion it is important to note that in contrast to "typical plant oils," where double bonds are "usually close to each other," in jojoba wax esters the double bonds "are far apart and uneven from the center." Ex. 2025, 9.

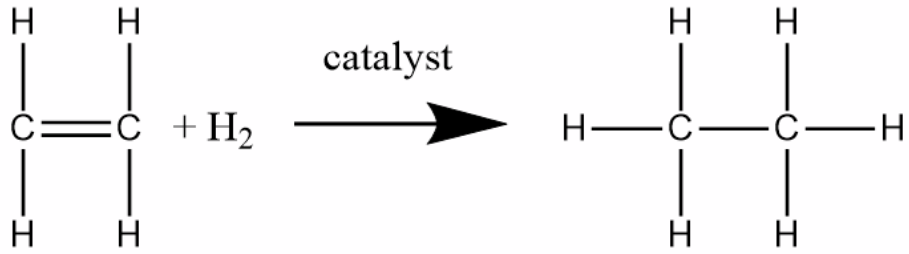
54. I note that a fatty acid chain may be saturated (meaning it contains no carbon-carbon double bonds), monounsaturated (meaning it contains a single carbon-carbon double bond), or polyunsaturated (meaning it contains multiple carbon-carbon double bonds). *See, e.g.*, Ex. 2026, 21; Ex. 2058, 1. A jojoba wax ester can only have two carbon-carbon double bonds, while triglycerides can have a

multitude of double bonds, depending on the composition of its three fatty acid chains.

55. In general, the more carbon-carbon double bonds that a fatty acid chain has, the lower that fatty acid chain's oxidative stability, or OSI, tends to be. That is because carbon-carbon double bonds are susceptible to oxidation. Ex. 2002, 5. A fully saturated fatty acid chain, meaning one that contains no carbon-carbon double bonds, is much less prone to oxidation and is therefore considered to be more stable. I note that an ester bond, meaning the double bond between the oxygen and the carbon, is incredibly stable, but eventually will oxidize given enough time and exposure to oxygen. Ex. 2020, 19.

56. In a triglyceride, the specific combination of fatty acids attached to the glycerol backbone determines the physical and chemical properties of the oil. Ex. 2027, 1. Natural oils with predominantly triglyceride structures include olive oil, sunflower oil, soybean oil, corn oil, palm oil, coconut oil, and peanut oil, among many others.

57. The saturation, or absence of double bonds, of a fatty acid chain can be increased through hydrogenation. A hydrogenation reaction involves the chemical addition of two hydrogen atoms to a carbon-carbon double bond, thus converting the "unsaturated" double bond into a "saturated" single bond, as shown below:

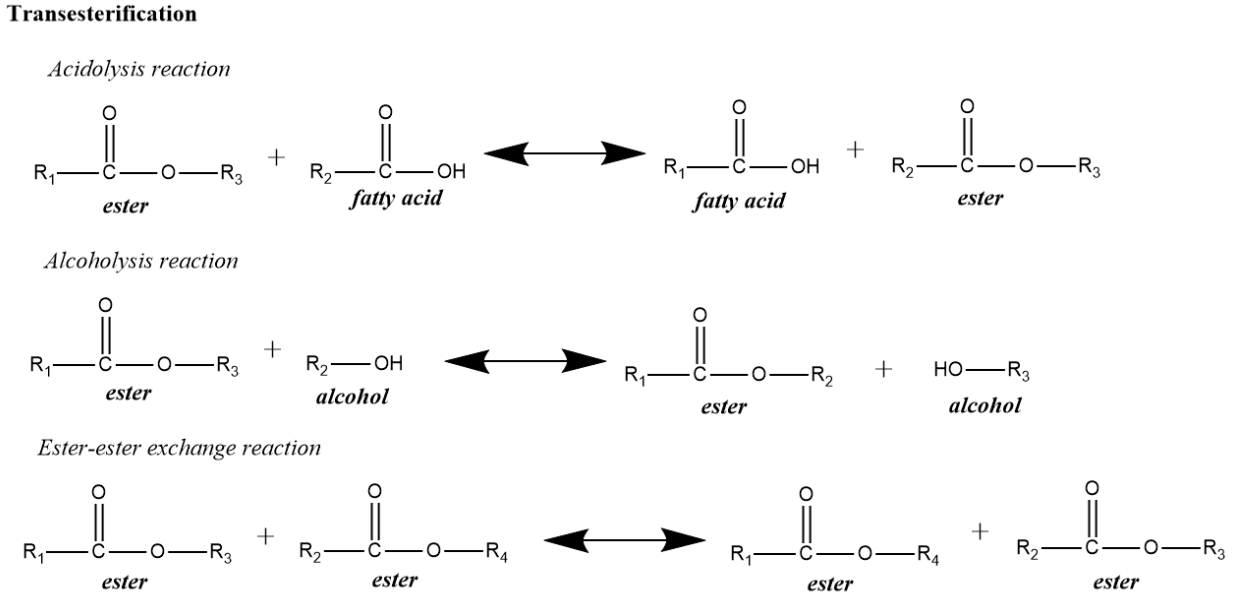



*See also* Ex. 2025, 10. Notably, hydrogenation results in a product with fewer double bonds.

### C. Transesterification of Wax Esters and Triglycerides

58. From my review of the literature, I understand that the terms transesterification and interesterification are often used interchangeably. Xu, one of the references cited in the Petition, uses the term interesterification as a general term for the following reactions: acidolysis, alcoholysis, and ester-ester exchange. Ex. 1008, 2. While Xu acknowledges that transesterification refers to the specific ester-ester exchange reaction, it also notes that the literature sometimes uses transesterification to mean "the acidolysis reaction or as a general term for all the three reactions including alcoholysis." Ex. 1008, 2. Other authoritative sources classify these two terms differently: transesterification is the broader term, with interesterification referring to ester-ester exchange. Ex. 2028, 4. To avoid confusion, throughout this declaration, I will endeavor to refer to transesterification as the broader term and interesterification as the narrower term, as this is also consistent with my reading of the '245 patent.

59. Transesterification reactions are classified into several categories, the more common being acidolysis, alcoholysis, and interesterification. The literature has classified all of these as transesterifications because there is an ultimate change in the ester structure. Ex. 2029, 1. I will provide a brief description of the various types of transesterification reactions, which are shown in the figures below:




In an acidolysis reaction, a fatty acid chain (R2-COOH) is reacted with an ester (R1-COO-R3) such that the R3 chain on the ester is replaced with the R2 group from the fatty acid chain, creating a new ester compound (R2-COO-R3) and a new free fatty acid product (R1-COOH). *See* Ex. 1008, 6. Similarly, in an alcoholysis reaction, an alcohol (R2-OH) is reacted with an ester (R1-COO-R3) such that one of the chains of the ester is replaced with the R2 group from the alcohol, creating a new ester compound (R1-COO-R2) and a new alcohol product (R3-OH). *Id*., 8. A new ester

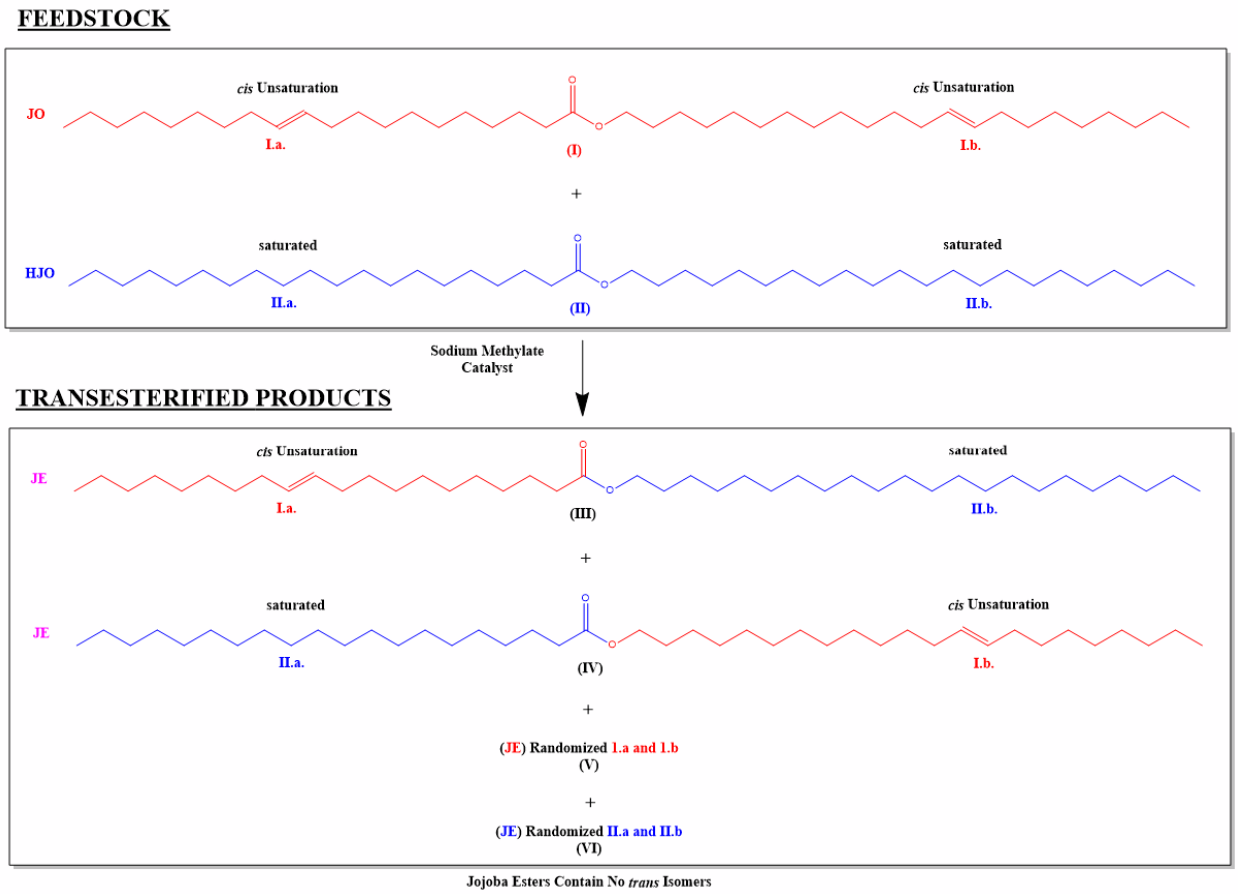
is formed in both acidolysis and alcoholysis with the new chains introduced by the fatty acid or alcohol. A new bond is formed at the carbonyl via a process termed 'nucleophilic attack,' which I will discuss more below. In acidolysis the nucleophile is the carboxylic acid with the R2, and for alcoholysis it is the alcohol with the R3.

60. Notably, in acidolysis and alcoholysis, both the free fatty acid and the alcohol end products are generally considered undesirable and therefore removed from the ester product in later processing steps. I note that this removal of the undesirable reaction products in alcoholysis and acidolysis reactions often leads to an increase in saturated product because double bonds are removed when those chains are transferred to the discarded alcohol or acid.

61. In an ester-ester exchange, a first ester (R1-COO-R3) is reacted with a second ester (R2-COO-R4) such that the chains on either side of each ester are swapped with one another, forming new esters (R1-COO-R4 and R2-COO-R3, among others). *See, e.g.*, Ex. 1014, 6. Notably, no new chains are added; the existing chains are rearranged instead. Additionally, in contrast to the acidolysis and alcoholysis reactions, depending on the esters used, an ester-ester exchange may not require the removal of any reaction products. For instance, no reaction products need to be removed in a jojoba wax esters reaction because both ester products are desirable reaction products. Indeed, an ester-ester exchange "only alters the distribution of the fatty acids over the triacylglycerols," and "[t]he stability of the oil

remains essentially unchanged[.]" Ex. 2030, 3. I note that the claims of the '245 patent are specifically directed to ester-ester exchanges. Ex. 1001, cl. 1.

62. Using an example, I will explain how ester-ester exchange can be used to randomize chains on two esters. Take jojoba wax esters, for instance. Prior to ester-ester exchange, jojoba wax esters predominantly have four potential configurations on either side of the ester bond—either both chains are C20, both chains are C22, or one C20 and one C22 chain. During ester-ester exchange, the combination of chains is randomized, as shown below:




Adapted from Ex. 1014, 6. The product of the ester-ester exchange between saturated and unsaturated jojoba wax esters is a randomized mixture of saturated

jojoba wax esters (II.a and II.b, above), the two monounsaturated jojoba wax ester species (I.a and II.b; II.a and I.b), and fully unsaturated jojoba wax esters (I.a and I.b).[1]

63. Now, in an ester-ester exchange with triglycerides, the three fatty acid chains can be exchanged not only on the same glycerol backbone, but also with fatty acid chains on other glycerol backbones in the same mixture, meaning there are even more potential combinations that can be created during the exchange. *See* Ex. 1008, 10-11.

### D. Prior Art Catalysts for Transesterification

64. Transesterification requires a catalyst to initiate the reaction. *See* Ex. 2030, 4 ("In the absence of a catalyst, even extreme conditions of temperature and time will not give the desired result."). Transesterification can be catalyzed by the addition of an acid or base catalyst, but can also be catalyzed with an enzyme catalyst. Ex. 2031, Abstract; Ex. 2032, Abstract. While chemical catalysts were known for use with both triglycerides and jojoba wax esters, enzymatic catalysts

[1] I note that in reality the mixture contains additional possible combinations based on the other potential chain lengths in the mixture (not pictured) that are shorter or longer than the 20 and 22 carbon chains.

such as lipases were understood in the art at the time of the invention to be specific to triglycerides. Ex. 2033, 1; Ex. 2035, 10.

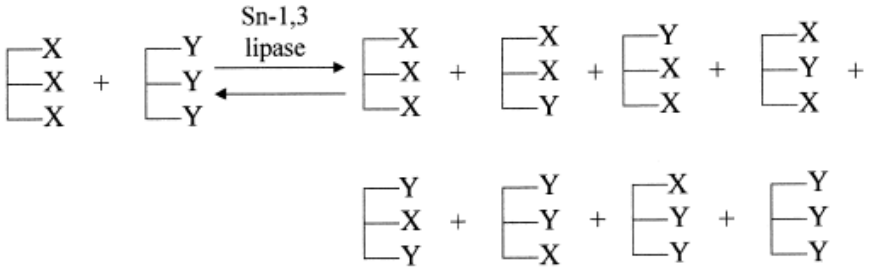
1. Chemical Catalysts for Transesterifying Triglycerides and Jojoba Wax Esters

65. Conventional catalysts used in the prior art primarily include base catalysts such as alkali metals (sodium, potassium and their alloys) and the corresponding alcoholates (sodium methylate and ethylate)[2]. *See* Ex. 2030, 1233; *see also* Ex. 1001, 3:66-4:1. Less commonly, acidic bentonite-type clay could also be used to transesterify wax esters. Ex. 1001, 3:53-63. The most common chemical catalyst in the prior art was sodium methylate.

66. Mechanistically, the chemical catalyst attacks the carbonyl group of one of the fatty acids of the triglyceride breaking the ester bond and freeing the fatty acid from the glycerol backbone. Ex. 2030, 5. As the reaction proceeds, the result will be either the fatty acid chains of the original triacylglycerol molecule remaining intact, or a new triacylglycerol molecule forming in which the fatty acid chains have been randomized. *Id*. Notably, with a triglyceride, transesterification can occur between the fatty acids on the same glycerol head or with fatty acids on other

[2] Sodium methylate and ethylate are interchangeable with sodium methoxide and ethoxide.

triglycerides in the mixture, leading to the creation of a multitude of different combinations and new triglyceride structures, as shown below.




X and Y are two types of fatty acids.

**Fig. 18.** Reaction scheme of enzymatic ester-ester exchange between two triacylglycerols (XXX and YYY) with *sn*-1,3 specific lipases.

Ex. 1008, 11.

67. A depiction of the chemical process is shown in the figures below.

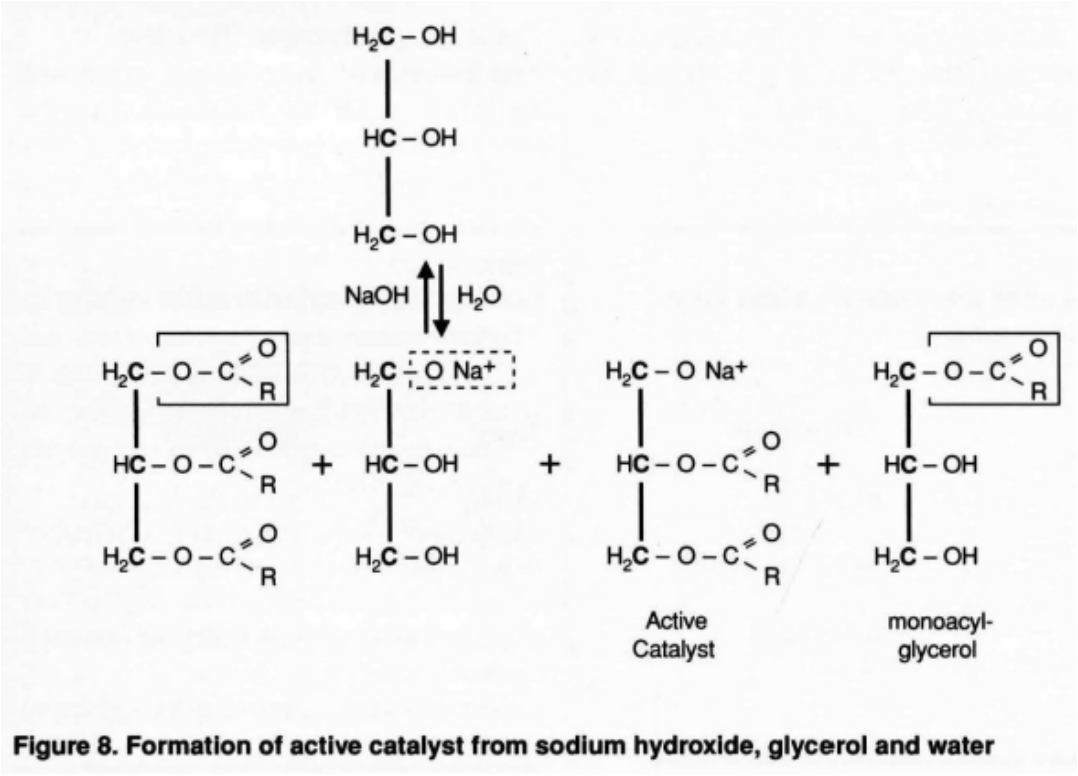



**Figure 8. Formation of active catalyst from sodium hydroxide, glycerol and water**

Ex. 2030, Fig. 8. Rozenaal's Figure 8 shows the basic chemical reaction when a base is used to transesterify a triglyceride. In this example, that base is sodium hydroxide, NaOH. The hydroxide (OH-) portion removes a hydrogen from glycerol to create its anionic form, i.e., glycerol-O- Na+ (a glycerol alkylate). This glycerol alkylate then 'attacks' the triglyceride (shown with the box drawn about it) to created a monoacyl glycerol, shown to the far right, and a diacyl-glyceride anionic form, labeled "Active Catalyst" which continues to react with other triacyl-glycerides forming randomized new esters. *Id.*, 5.

68. The figure below illustrates the interesterification of a triglyceride with glycerol, using the anion formed above as the chemical catalyst.

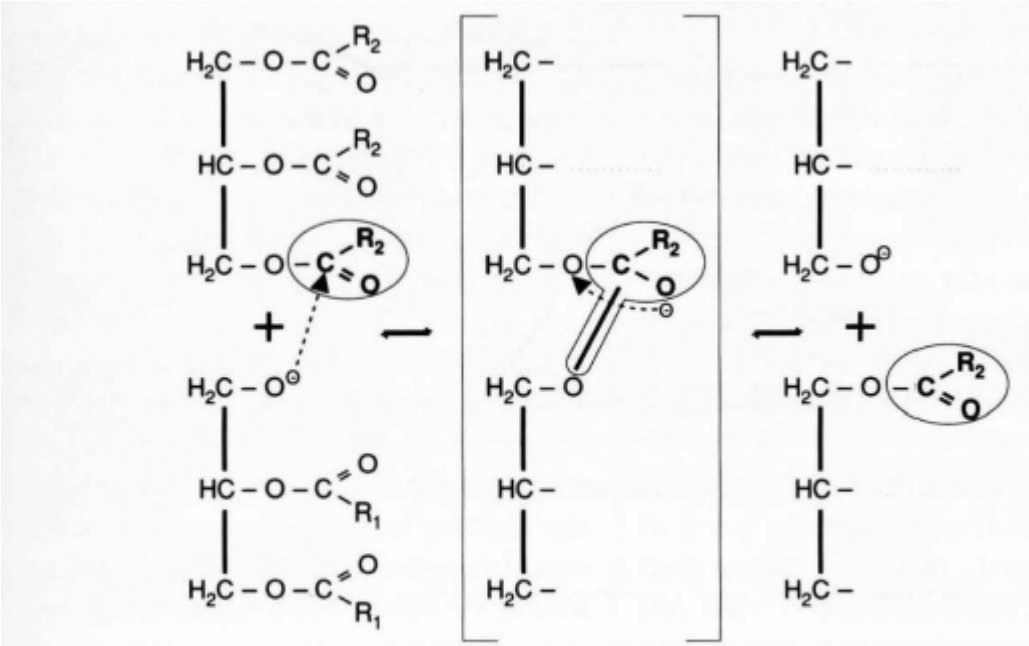


**Figure 9. The mechanism of interesterification**

Ex. 2030, Fig. 9. This glycerol anion transesterifies the triglyceride.

2. Enzymatic Catalysts for Transesterifying Triglycerides

69. Enzymatic transesterification, by contrast, uses enzymes instead of a chemical catalyst to facilitate the reaction. Broadly speaking, enzymes are proteins (made up of amino acids) that act as catalyst, causing or accelerating a reaction to replace acids and bases needed in chemical synthesis. Ex. 2059, 1-2. An enzyme acts on a substrate (i.e., a chemical compound or molecule) to modify the compound or molecule to create a new product. *Id.*, 2. An enzyme is comprised of different protein domains, and contains at least one active site, which is where the enzyme binds the substrate and catalyzes the reaction. *Id.* The active site is sometimes referred to as the "catalytic domain" because that is where a reaction is catalyzed. Ex. 2035, 2. The interaction between an enzyme and its substrate is highly specific, as the active site's shape and chemical properties are precisely tailored to accommodate the substrate. The active site also forms a microenvironment, or pocket, that stabilizes the transition state of the substrate as it is modified, reducing the amount of energy required for the reaction to occur and thus causing the reaction to speed up. Ex. 2037, 1; Ex. 2035, 3. Additionally, the active site may contain amino acids that form temporary bonds with the substrate to help facilitate the reaction. Ex. 2037, 2; Ex. 2035, 4. In general, the specificity and efficiency of enzymes largely depends on the characteristics and structure of their active sites.

70. Lipases are a specific class of enzymes that were known, at the Critical Date, to perform a number of reactions, including catalyzing the hydrolysis of triglycerides. Ex. 2038, 2. In hydrolysis, a lipase converts a triglyceride into di-/mono-glycerides, fatty acids, and glycerol. *Id.* Lipases were also known to catalyze transesterification reactions, including ester-ester exchanges (i.e., interesterification reactions). *Id.*

71. At a high level, lipase-catalyzed interesterification occurs largely in two steps, resulting from the interaction between the lipase and reactants: first, carboxylic ester bonds are hydrolyzed, then esters are re-synthesized by the esterification of reaction intermediates. *See* Ex. 2036, 2; *see also* Ex. 2028, 19; Ex. 1029, 1, Ex. 1016, [0024]. In the next sections, I provide more detail on the various type of lipases and how lipases mechanistically catalyze transesterification reactions.

***a. Overview of Lipases***

72. Lipases are categorized as enzymes that are specific to glycerides, and are more specifically defined as triacylglycerol acylhydrolases. Ex. 2039, Abstract; Ex. 2028, 1. Lipases target triacylglycerols (i.e., triglycerides) and require its substrate to be a triester based on a 1,2,3 triol backbone (i.e., glycerol) to match up with the reaction site. Ex. 2028, 2.

73. Lipases exhibit various types of activity to mono-, di-, and triglycerides, including: (1) type-selectivity, (2) regioselectivity, and (3) enantioselectivity, *See*

Ex. 2063, 2, 5; Ex. 1029, 2 ("other catalysts which have enabled transesterification to be highly efficient and chemo-, stereo-, and regioselective."), 14 ("enzymatic transesterification is attractive in terms of specificity"). Type-selectivity is associated with the lipase's preference for a particular substrate, such as tri-, di-, or monoglycerides, fatty acid chain length, and degree of unsaturation. Ex. 2028, 14.

74. Regioselectivity is defined by the preferential action of a lipase on a specific ester bond in the glycerol backbone of triglycerides (e.g., *sn*-1(3) or *sn*-2). Ex. 2011, 4; Ex. 2028, 15. *Sn*-1,3-specific lipases, for instance, display regioselectivity because they release fatty acids from the *sn*-1 and *sn*-3 positions of a glyceride, but do not affect the *sn*-2 position. Ex. 2033, 7. Non-specific lipases, by contrast, do not display any regioselectivity towards the *sn*-1 and *sn*-3 positions of a glyceride; instead, they randomly cleave fatty acid molecules at any of the three ester positions to generate free fatty acids, glycerol, and mono- and diglyceride intermediates. *Id.* Importantly, both *sn*-1,3 lipases and non-specific lipases bind to the glycerol backbone of a triglyceride. *Id*.

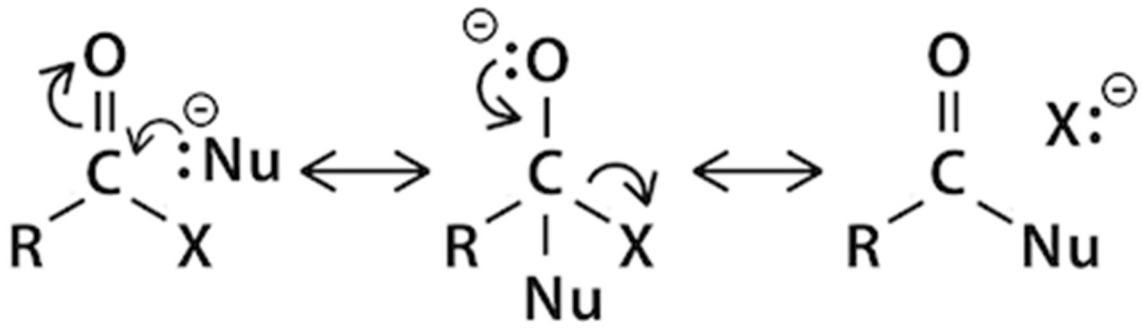
75. As the name would suggest, enantioselectivity is defined as a preference towards certain competing enantiomeric substrates. Enantiomers are pairs of molecules that are mirror images of each other. Controlling lipase enantioselectivity for organic synthesis involves proper alignment within the lipase's

reaction site, similar to a left handed glove fitting only the left hand. *See* Ex. 2040, 2; Ex. 2041, 1.

***b. Lipase-Catalyzed Transesterification of Triglycerides***

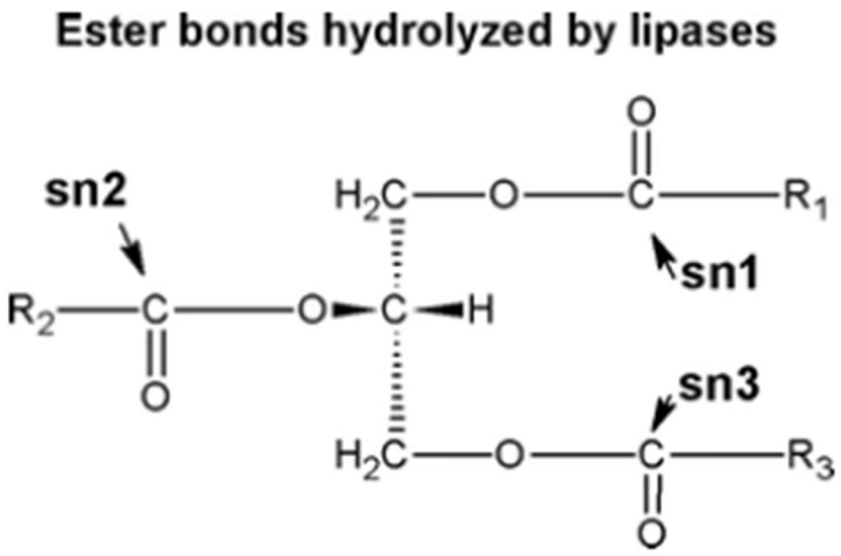
76. All of the prior art references disclosing enzymatic transesterification deal with transesterification of triglycerides using a lipase. This makes sense, given that lipases convert a triglyceride into di-/mono-glycerides, fatty acids, and glycerol, or into other triglycerides via interesterification. Ex. 2038, 1. Even the '245 patent notes this: "[l]ipases like those disclosed herein are conventionally used for processing triglycerides." Ex. 1001, 14:24–25. As detailed below, after a thorough literature review, I have found that, prior to 2014, scientists had only utilized lipases to transesterify triglycerides, and not jojoba wax esters. As described above, jojoba wax esters are not triglycerides. I have found no publications or patents prior to 2014 that show using lipases to transesterify jojoba wax esters, and I note that Dr. Rockstraw has not identified any such references either.

77. The literature demonstrates that, regardless of type-, regio-, or enantio-selectivity, lipases exhibit very specific interactions with triglycerides. The reaction within the lipase's catalytic domain (i.e., reaction site) is termed a "nucleophilic substitution." This is shown below:




Ex. 2019, 2-3. Nucleophilic substitution is a major concept in organic chemistry. A nucleophile is defined as a molecule having a negative charge due to a pair of non-bonding electrons on one atom. The negative charged species moves, or attacks, a potentially positive atom. *Id.*, 3; Ex. 2024, 3. In ester synthesis the potentially positive site is the carbonyl, C=O, which exists in an 'enol' form and is represented as C(+)—O(-). The nucleophile (Nu:) attaches to the C(+) and then the O(-) forces the departure of the X: via bond scission forming the new structure.

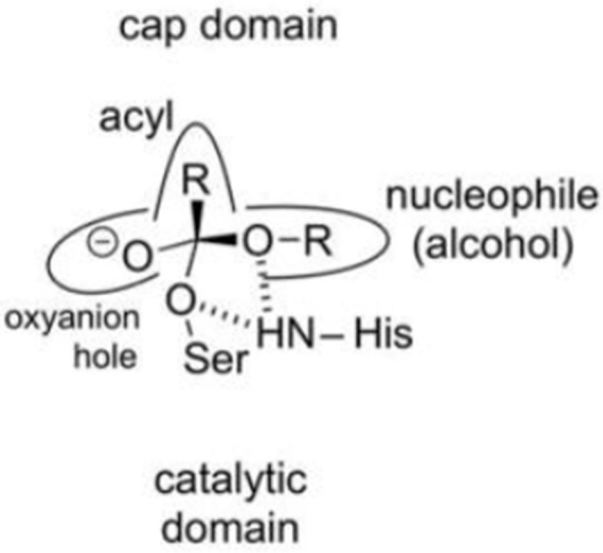
78. To perform nucleophilic substitution, lipases are specifically tailored to react with triglycerides, as shown below:




The nucleophilic substitution within a triglyceride by a specific *sn*-1,3 lipase, for example, involves the carboxylic acid bond scission at the *sn*-1 carbonyl with ester rearrangement to the *sn*-3 position. In this reaction, specific amino acids at the catalyst site act as transitional aids to enable the glycerol to act as a nucleophile facilitating the transesterification of R(1)—CO from the *sn*-1 to the *sn*-3 site.

79. The reaction site of a lipase, sometimes referred to as the catalytic domain, comprises an oxyanion hole, a catalytic triad, and a beta sheet. This core catalytic domain interacts with triglycerides in a specific manner to catalyze the ester-ester exchange. Ex. 2035, 3. The catalytic triad contains three amino acid residues: serine ("Ser"), histidine ("His"), and aspartic acid ("Asp"). *Id.* Two of the three oxygens present in the glycerol head of a triglyceride bind the N-H groups present in the Ser-His-Asp catalytic triad of the lipase. *Id.* This binding creates an

oxyanion hole in which the triglyceride/Ser-His-Asp binding stabilizes the triglyceride tetrahedral intermediate as the ester-ester exchange occurs. *Id.* The interaction between the catalytic triad and the triglyceride substrate is shown below:

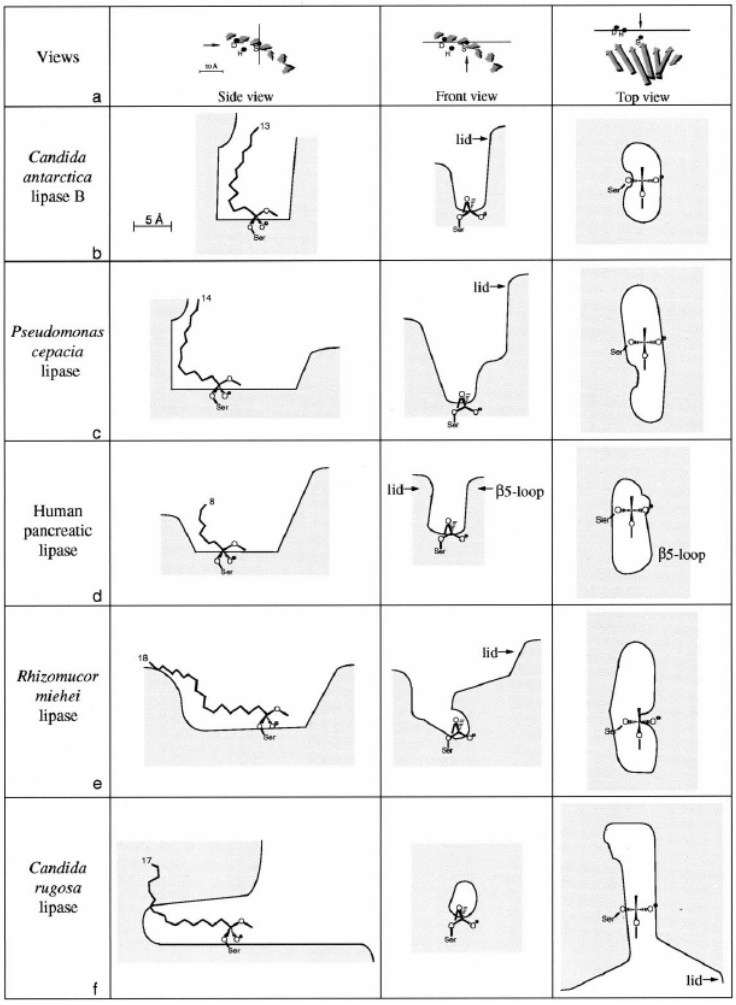



Ex. 2035, Fig. 2

80. The beta sheet of the lipase further stabilizes the triglyceride as ester-ester exchange ensues. Briefly, a beta sheet is a common component of a protein that confers structure and folding. In the context of a lipase, the beta sheet binds the C-9 and C-12 carbons of the fatty acid chain, thereby stabilizing the triglyceride molecule during ester-ester exchange. Ex. 2028, 8.

81. Additionally, the geometries of the lipase binding sites can also affect the ability of the triglyceride to bind. The geometries can be crevice-like, funnel-like, or tunnel-like, and the length of the binding site can vary between lipases. Ex. 2063, 1, 8; Ex. 2028, 12-13. To illustrate, the below figure shows various lipases

binding with triglyceride molecules in the catalytic/lid regions, with the number at the end of the fatty acid chain indicating the length of the longest fatty acid which binds inside the binding pocket. Ex. 2063, 3.



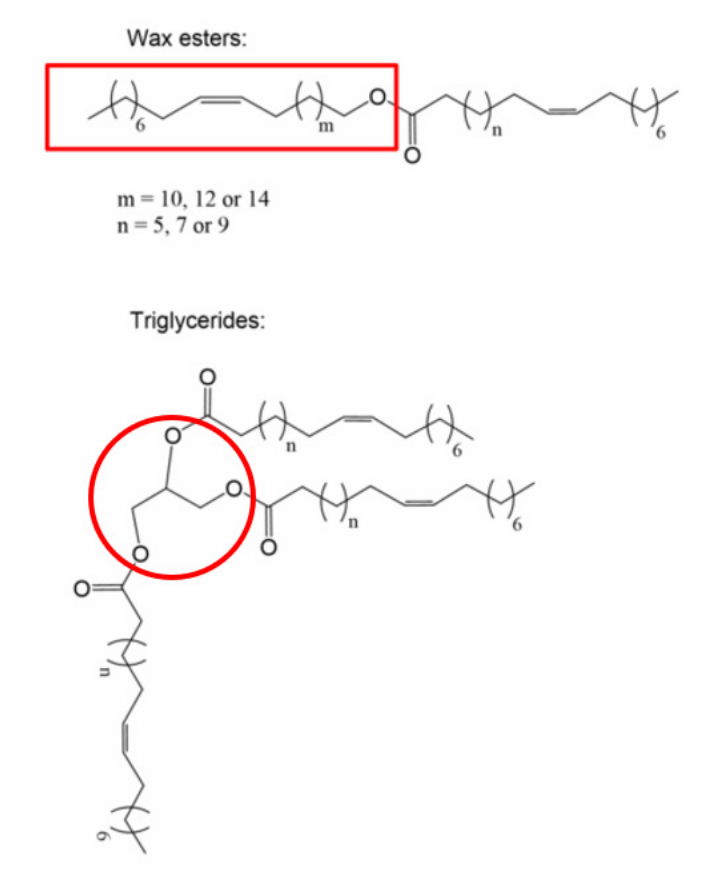

Ex. 2063, FIG. 1.

The above figure shows the binding site shapes of various lipases, including various cross-sections to illustrate the shape of the binding site from a side, front and top view. *See* Ex. 2063, 3, Fig. 1. The number in each figure indicates the length of the longest fatty acid that can completely bind inside the binding pocket. *Id.* Notably,

the longest fatty acid chain identified is 18 carbons. *Id*. The various geometries of the lipases' binding sites would have created additional specificity for binding triglycerides.

### *c. Lipases Would Not Be Expected to Transesterify Jojoba Wax Esters*

82. As I discuss above, structurally speaking, jojoba wax esters are very different from triglycerides. Shown below are illustrations of the chemical structure of a jojoba wax ester and a triglyceride, with a red box drawn around the alcohol moiety of each molecule. As can be seen in the illustrations, the alcohol moiety of the jojoba wax ester is very large (22 carbons), whereas the alcohol moiety of the triglyceride molecule comprises just three carbons on the glycerol side.




83. These structural differences would have been expected to negatively impact a lipase's ability to bind a jojoba wax ester. In my opinion, such expected negative impacts on binding would have caused a person of skill in the art to believe that jojoba wax esters were an unsuitable candidate for lipase-catalyzed transesterification.

84. Specifically, the structural differences from triglycerides would be expected to affect a jojoba wax ester's ability to fit into the core catalytic domain of the lipase. As I described above, lipases are typically highly specific as to the substrates they efficiently catalyze; this specificity is dictated by the size, shape, and

other characteristics of the triglyceride binding site of the particular lipase. Ex. 2063, Abstract. It would not be expected that a jojoba wax ester could fit within the restricted space of the enzyme's reaction site due to the steric hindrance resulting from its large alcohol chain and its acid chain extending in the opposite direction from the ester group. Ex. 2063, Fig. 1.

85. Lipase selectivity would also counsel against successfully transesterifying jojoba wax esters using lipases. As I discussed above, lipases display regioselectivity in the preferential action of lipases on a given ester bond of a substrate, particularly in the glycerol backbone of triglycerides (e.g., *sn*-1,3 specific lipases preferentially react with acyl groups at the *sn*-1 and *sn*-3 positions of glycerol). Ex. 2028, 15. Jojoba wax esters, however, do not contain glycerol backbones (see figure above). Therefore, they do not have an *sn*-1 or *sn*-3 position like a triglyceride does. As a result, *sn*-1,3 lipases simply would not be expected to catalyze an ester-ester exchange using jojoba wax esters as a substrate. Similarly, non-specific lipases, which (as discussed above) do not display any preference for the three fatty acid chains of a triglyceride, still rely on the general configuration of the three *sn*-1, *sn*-2, and *sn*-3 positions, and would not be expected to transesterify jojoba wax esters due to their chemical difference from triglycerides (and their lack of sn-1, 2, or 3 positions).

86. Lastly, the expected interactions between the lipase's catalytic machinery and jojoba wax esters are not comparable to that of triglycerides. As discussed above, the lipase's reaction mechanism requires, *inter alia*, the catalytic triad (Ser-His-Asp), which forms the oxyanion hole when the substrate binds. Ex. 2035, 2. Unlike a triglyceride, which has three oxygens within the glycerol head to bind the catalytic triad, jojoba wax esters only have one available oxygen on the alcohol side of the ester (see figure above). This would mean that a jojoba wax ester with only this single point of contact with the catalytic triad, instead of three as in a triglyceride, would result in the jojoba wax ester being less capable of coordinating with the oxyanion hole. *Id.* A person of ordinary skill in the art would have expected that having less stability within the catalytic site would render the jojoba wax ester incapable of being transesterified with the lipase.

87. I note that the '245 patent discussed the low odds of jojoba wax esters successfully undergoing transesterification using a lipase. "Interestingly, both 1, 3 lipases and lipases that operate using insertion of a triglyceride work equally well when used in jojoba ester transesterification reactions. This result is unexpected, as these lipases sterically interact quite differently with the molecules they are involved in catalyzing." Ex. 1001, 14:38–42.

## VI. THE ’245 PATENT

### A. Overview of Patent

88. I have reviewed the ’245 patent (Ex. 1001) in detail. The ’245 patent described for the first time methods and experimental results demonstrating that jojoba wax esters could be successfully transesterified using a lipase. Ex. 1001, 1:22-28. The ’245 patent notes that transesterification of the jojoba wax esters “permits altering of various physical properties of the transesterified product when compared to the original feedstock,” including properties like viscosity, dropping point, oxidative stability index (OSI), carbon chain distribution, and others. *Id*., 3:38-46. It further explains that “[t]hese changes take place at least in part because the chain lengths of the resulting ester products are randomized compared to the distribution in the original wax ester feedstock, which may alter the functionality of the transesterified material in a mixture and/or the thermal properties of the material.” *Id*., 3:46-51.

89. In the process of transesterifying a wax ester feedstock using enzymatic catalysis (illustrated in Fig. 2, which I have reproduced below), the ’245 patent explains that a “wax ester feedstock passes through one or more catalytic reactors that allow a continuous catalytic transesterification reaction to take place.” *Id*., 5:1-3. Notably, the use of enzymatic catalysis in transesterification of wax esters

has “fewer process steps” than chemical catalysis and leads to “little or no side reactions between the enzyme catalysts and the reactants.” *Id*., 5:9-13.

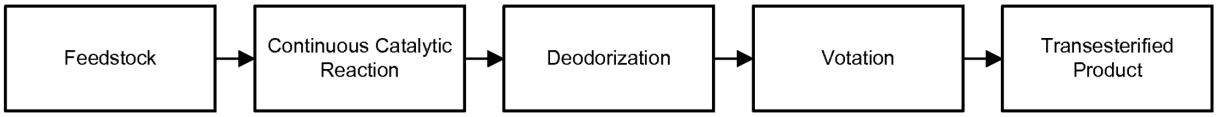



FIG. 2

Ex. 1001, Fig. 2.

90. I note that the ’245 patent discloses numerous unexpected and surprising results when an enzyme catalyst is used instead of a chemical catalyst, including improvements in OSI, viscosity, and performance. First, the ’245 patent compares chemical and enzymatic ester-ester exchange by applying both processes to refined jojoba wax esters (i.e., fully unsaturated oil). *Id*., 8:41-67 (Example 1). The results of the ester-ester exchange are shown in Table 3:

TABLE 3

| | Feedstock Composition | Chemical Catalyst | % Change | Enzyme Catalyst | % Change |
|---|---|---|---|---|---|
| Components | | | | | |
| Tocopherols | 0.04% | 0.00% | −0.04% | 0.04% | 0.00% |
| Fatty Acid Methyl Esters | 0.00% | 3.10% | 3.10% | 0.00% | 0.00% |
| Free Fatty Alcohols | 0.00% | 1.80% | 1.80% | 0.00% | 0.00% |
| OSI (hours) | 26.5 | 21.5 | −18.87% | 38.6 | 45.66% |
| Wax Ester Content | 98.00% | 93.10% | −4.90% | 98.00% | 0.00% |
| Wax Ester Distribution | | | | | |
| C36:1 | 1.12% | 1.30% | 0.180% | 1.20% | 0.080% |
| C38:2 | 6.02% | 4.90% | −0.120% | 4.80% | −1.220% |
| C40:2 | 27.95% | 35.76% | 7.810% | 34.34% | 6.390% |
| C42:2 | 50.28% | 40.64% | −9.640% | 40.92% | −9.360% |
| C44:2 | 9.94% | 13.75% | 3.811% | 14.93% | 4.991% |
| C46:2 | 1.20% | 1.89% | 0.690% | 2.23% | 1.030% |

91. As shown in Table 3, the original feedstock had an oxidative stability (OSI) of 26.5 hours. *Id*., 9:26-47. When chemically transesterified, the OSI of the product dropped by ~20% to 21.5 hours. *Id.* The '245 patent notes that the chemically catalyzed reaction "destroys the original amount of tocopherols present in the feedstock, which reduces the OSI of the transesterified product." *Id*., 9:53-56. I note that tocopherols are a vitamin E derivative and are one kind of antioxidant that can be added to increase the OSI of a mixture. Ex. 2042, 2. Additionally, I note that fatty acid methyl ester and free fatty acid byproducts were formed through chemical transesterification. Ex. 1001, 9:49-53. On the other hand, when the feedstock was enzymatically transesterified using a lipase, the OSI of the product increased by 45% to 38.6 hours—a quite surprising result that, in my opinion and as noted by the '245 patent, cannot be explained simply by the preservation of tocopherols. *Id*., 9:26-47;

*see also id.*, 9:58-62 ("This result indicates that the enzymatic catalysis has an unexpected positive effect on OSI that is not explainable simply by the enzymatic catalyst preserving the natural tocopherols originally present in the feedstock during the reaction."). I note that this surprising result was repeated in a second experiment that used a continuous flow reactor rather than a batch reactor. *See id.*, 11:38-12:24; *id.*, 12:18-20 ("Again, the increase in OSI from the feedstock material was again surprisingly noted.").

92. In addition to the unexpected increase in OSI, the '245 patent provides further evidence demonstrating that the enzymatically transesterified product surprisingly performed better than the chemically transesterified product. Both wax ester products were tested for their performance in a "typical cream formulation" shown in Table 4, with all components kept the same apart from the transesterified product. *See id.*, 10:5-67. Table 5, which I have reproduced below, shows the results of the comparison:

TABLE 5

| Transesterified Product Type in Cream | Viscosity | Appearance |
|---|---|---|
| Chemically Catalyzed | 120,900 cP | White, semi-solid phase |
| Enzymatically Catalyzed | 78,585 cP | White, liquid phase, glossy |

Ex. 1001, 11:17-25. Surprisingly, the enzymatically transesterified product created a cream formulation that "had a viscosity drop of nearly 35%" from the viscosity of the formulation prepared with the chemically transesterified product. *Id.*, 11:17-29.

Further, the ’245 patent noted a significant difference in the creams’ appearances, with the cream derived from chemical transesterification having a “[w]hite, semi-solid phase” appearance, while the cream derived from enzymatic transesterification had a “[w]hite, liquid phase, glossy” appearance. *Id*., 11:17-24; 12:20-24.

93. Despite these differences, the ’245 patent goes on to demonstrate, surprisingly in my opinion, that the enzymatically and chemically transesterified wax esters nevertheless had nearly the same distribution of fatty acid chains, as shown in Figure 4:

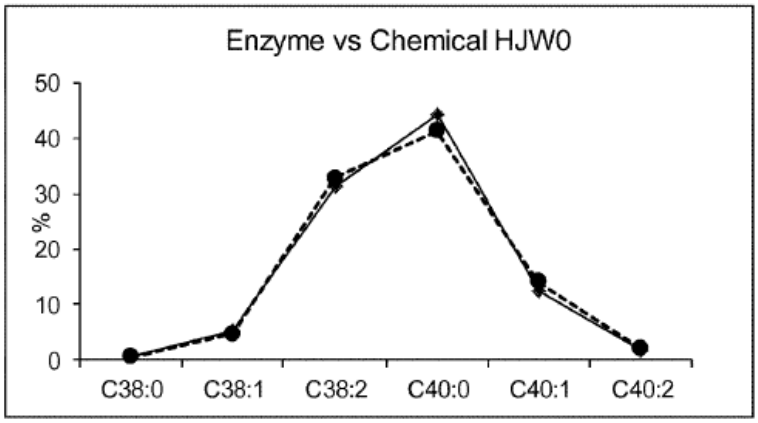



FIG. 4

*Id*., Fig. 4 (solid line = chemical; dotted line = enzymatic). The ’245 patent notes that “[b]y observation, it is clear that the enzymatically catalyzed process successfully randomizes the various esters very similarly to the chemically catalyzed process.” *Id*., 14:10-12. Thus, the differences in performance and physical properties do not appear to be attributable simply to differences in the underlying chemical structure of the respective esters. *See id*., 14:19-23.

94. The ’245 patent also describes preparing jojoba wax esters by transesterifying refined jojoba wax esters with 20%, 30%, and 50% fully saturated (i.e., hydrogenated) jojoba wax esters (HJW). Figures 5 through 7 demonstrate that, just as with transesterifying jojoba wax esters alone, transesterifying with hydrogenated feedstock resulted in the same distribution of fatty acid chains:

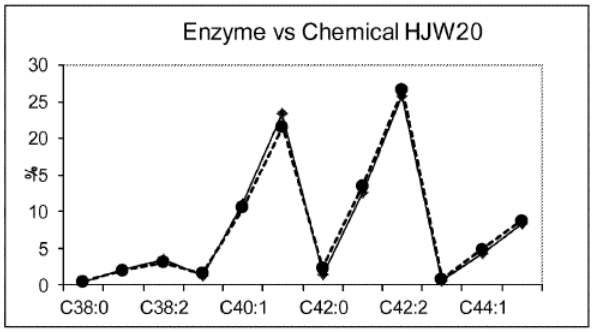



FIG. 5

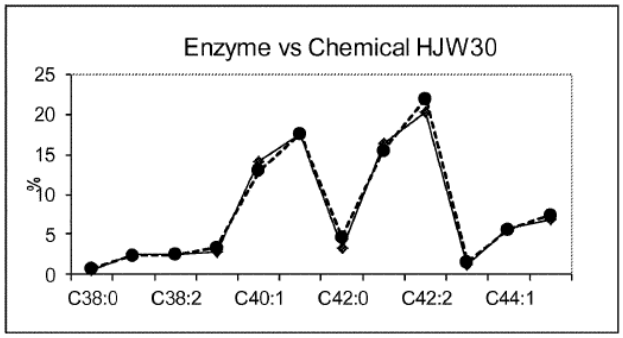



FIG. 6

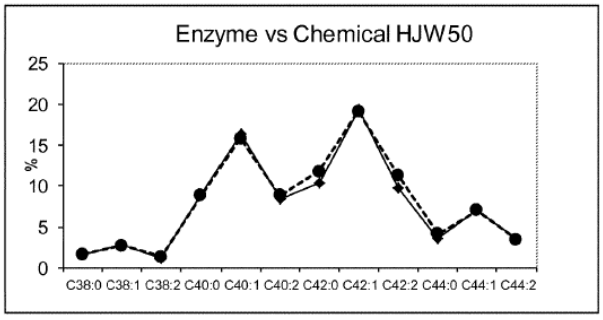



FIG. 7

*Id*., Figs. 5-7; *see also id.*, 14:12-19.

95. I note that the ’245 patent also discusses unexpected differences between using a lipase on triglycerides and using a lipase on jojoba wax esters. In my opinion, it was very unexpected at the time of the invention that a lipase would work at all on jojoba wax esters because jojoba wax esters do not have a glycerol backbone, as I discussed in detail above. *See* Section V(B). The ’245 patent notes

the additional surprising result in that jojoba wax esters could be transesterified by different kinds of lipases, including both *sn*-1,3 lipases and non-specific lipases—which I note the '245 patent refers to as "lipases that operate using insertion of a triglyceride." *Id*., 14:38-40. The '245 patent notes (and I agree) that "[t]his result is unexpected, as these lipases sterically interact quite differently with the molecules they are involved in catalyzing." *Id*., 14:40-42; *see also id.*, 14:51-54 ("As this processing characteristic for lipase catalytic processing of jojoba wax esters is not a predictable result, this illustrates a unique aspect of processing jojoba wax esters using lipases.").

96. In addition to discovering that lipases unexpectedly worked with jojoba wax esters, I note that the inventors also discovered that when lipases work with jojoba wax esters, the reaction produces results that are not observed with triglycerides. That is, enzymatic transesterification of jojoba wax esters as compared to enzymatic transesterification of triglycerides generates significantly greater production volumes. For instance, while "conventional processing of triglycerides" with lipases "typically yields up to 4000 kg of product per kg of catalyst," when lipases were used with jojoba wax esters instead, "a kg of product to kg of catalyst ratio of 5011" could be achieved, that is, "over 20% greater than the ratio when the same lipase is used for triglyceride production." *Id*., 14:55-15:8. This result "significantly exceeds the conventional expectations for the lipase, and is an

unexpected result that is not predicted by the results of conventional enzymatic triglyceride processing." *Id*., 15:8-12. Thus, it is surprising to me that, in addition to being able to react with jojoba wax esters at all, using lipases with jojoba wax esters somehow resulted in even higher productivity than was observed with triglycerides.

97. In my opinion, these various unexpected results, achieved using a novel lipase-based process to enzymatically transesterify jojoba wax esters, further illustrate the novelty and non-obviousness of the claimed invention.

### B. Patent Claims

98. The '245 patent includes 1 independent claim and 4 dependent claims. The independent claim describes a process for transesterifying wax esters:

> 1. A process for transesterifying wax ester, the process comprising:
>
> [1a] providing a feedstock comprising jojoba wax esters and hydrogenated jojoba wax esters, wherein the amount of hydrogenated jojoba wax esters is 20 % to 50 % by weight of the feedstock;
>
> [1b] contacting the feedstock with a lipase; and transesterifying the jojoba wax esters and the hydrogenated jojoba wax esters in the feedstock with the lipase to form a transesterified product;
>
> [1c] wherein an oxidative stability index (OSI) of the transesterified product is greater than an OSI of the feedstock.

99. I use the above indicators [1a]-[1c] (as shown above) to identify the limitations of the independent claim throughout this Declaration.

100. The dependent claims 2-5 specify additional aspects of the claimed process of the independent claim:

> 2. The process of claim 1, wherein the feedstock consists essentially of the jojoba wax esters and the hydrogenated jojoba wax esters.
>
> 3. The process of claim 1, wherein the feedstock does not comprise any free fatty alcohols.
>
> 4. The process of claim 1, wherein the transesterified product does not comprise any methyl esters.
>
> 5. The process of claim 1, wherein the feedstock does not comprise any methyl esters.

101. I note that Vantage has not challenged claim 4 in this proceeding.

### C. The Prosecution History of the ’245 Patent

102. I understand that the application that ultimately issued as the ’245 patent was filed on December 19, 2014, and underwent extensive prosecution over a nearly eight year period. I understand that the Examiner reviewed over one hundred prior art references and issued eight separate rejections using eleven different references. Additionally, I understand that the Examiner considered four different declarations submitted by first named inventor, Jeff Addy, to support the unexpected results demonstrated in the specification. I have reviewed the Examiner’s rejections, the applicant’s responses, and the Addy declarations as part of my work in this matter.

103. Throughout prosecution, I understand that the Examiner issued multiple rejections over prior art that disclosed lipase-catalyzed alcoholysis reactions in triglycerides. These rejections relied on the premise that the "OSI of the trans-esterified product being greater than an OSI of the feedstock is a property that would necessarily be presented in the process as taught by [the prior art] because the prior art method steps are the same as recited in the instant claims." Ex. 1002, Pt. 2, 425; *see also id.*, 426-427; *id.*, Pt. 3, 555; *id.*, Pt. 4, 766, 814, 972-973; *id.*, Pt. 5, 1035, 1123-1124. In other words, the Examiner argued that enzymatic transesterification inherently results in a transesterified product with an OSI greater than the OSI of the feedstock. I note that this is not true, as the applicant was able to demonstrate.

104. The Examiner appears not to have appreciated two important features of these references until the end of prosecution. First, that there is an important distinction between an alcoholysis transesterification and the ester-ester exchange transesterification required by the claims, as I describe in Section V(C) above. Second, that even in an alcoholysis transesterification, OSI of the product was not always greater than the OSI of the feedstock. Indeed, in my opinion the OSI of the product would generally only be expected to increase if the alcohol reaction products were removed. I discuss these two points in more detail below.

105. I note that most of the prior art that formed the basis of the Examiner's rejections used an alcoholysis transesterification, rather than the ester-ester exchange required by the claims. As I explained above, in an alcoholysis reaction, an alcohol is reacted with an ester such that the fatty acid chain attached to the alcohol is swapped with one of the ester's side chains. *See* Section V(C). The resulting unwanted end product, with the alcohol attached to the ester's lost side chain, is generally removed in a later process step from the desired ester product. Ex. 2043, 81; Xu, Ex. 1008, 9. As such, alcoholysis can be used to remove side chains that are unsaturated or partially unsaturated (i.e., have double bonds). Removing chains with double bonds would generally have been expected to improve the OSI of the oil by reducing the number of double bonds in the product susceptible to oxidation. In other words, when used in the context of removing unsaturated or partially unsaturated side chains of an ester reactant, alcoholysis would generally have been expected to reduce the amount of unsaturation in the ester product and improve the oxidative stability.

106. But I note that even in an alcoholysis reaction, different results could be achieved, as was demonstrated during prosecution. Inventor Jeff Addy replicated two alcoholysis reactions from the prior art and compared the results using jojoba wax esters with results using a triglyceride-based oil. First, Addy replicated the protocol disclosed in Steinke. Ex. 2045. I note that Steinke used lipase-catalyzed

alcoholysis on crambe oil and camelina oil but disclosed no oxidative stability data. Addy replicated Steinke's protocol using crambe oil and jojoba oil (i.e., jojoba wax esters), noting that both of these materials have similar qualitative properties, including "iodine values between 65-67" and "similar oxidative parameters in [peroxide value] and [anisidine value] prior to the reaction." Ex. 1002, Pt. 2, 469. Given these similarities, Addy stated (and I agree) that "one would expect the OSI of the crambe and jojoba derivatives be close if not identical." *Id*., 470.

107. But when Addy tested the OSI of the feedstocks and transesterified products from Steinke's alcoholysis method, he surprisingly found a different result between jojoba oil and crambe oil. While jojoba oil had over a three-fold increase in OSI, crambe oil had an increase of only about an hour:

| OSI (hours) | 1 | 2 | 3 | Avg. | +/- |
|---|---|---|---|---|---|
| Jojoba Pre-Reaction | 15.825 | 18.176 | 18.484 | 17.495 | 1.455 |
| Jojoba Post Reaction | 65.075 | 68.875 | 67.775 | 67.242 | 1.955 |
| % Change | 411% | 379% | 367% | 384% | 23% |
| | | | | | |
| Crambe Pre-Reaction | 1.191 | 1.134 | 1.765 | 1.363 | 0.349 |
| Crambe Post Reaction | 2.537 | 1.990 | 2.635 | 2.388 | 0.348 |
| % Change | 213% | 176% | 149% | 175% | 32% |

Ex. 1002, Pt. 2, 467-468. Addy explained to the Examiner that a one hour difference in OSI is within the margin of testing error and would not have been considered meaningful under Steinke. *Id*., 469. Addy concluded that using Steinke's method did not always result in transesterified products with improved OSI over the feedstock, and thus whether a particular "feedstock material will demonstrate the

OSI increase following enzymatic transesterification reaction is not predictable using these common parameters." *Id*., 470. I understand that the Examiner subsequently withdrew the rejections over Steinke.

108. I note that the unpredictability of the enzymatic transterification was further supported by another declaration that Addy submitted that replicated a method from Gunawan. *Id*., Pt. 3, 554-558; *id*., Pt. 2, 426-427; Ex. 2045. Just as with Steinke, Addy replicated Gunawan's lipase-catalyzed alcoholysis reaction using jojoba oil and sunflower oil, a common triglyceride-based oil. *See* Ex. 1002, Pt. 4, 838-843. Surprisingly, Addy found that while the OSI of the transesterified sunflower oil (Experiment 1) increased slightly over the OSI of the feedstock, transesterified jojoba oil (Experiment 2) had the opposite result, demonstrating decreased OSI compared to the feedstock:

| | Experiment 1 | Experiment 2 |
|---|---|---|
| Reactants OSI (hrs) | 5.8 | 24.0 |
| Products OSI (hrs) | 7.0 | 18.0 |
| Δ % | 20.7 | -25.0 |

**Table 4**. Oxidative Stability Index of Experiments 1 & 2

*Id*., 841. Thus, Addy concluded (and I agree) that "the observed failure of the method of Gunawan to produce a product with a higher OSI when jojoba oil was used as the feedstock demonstrates that, in my opinion, it would be impossible for a person of ordinary skill reading Gunawan to have had any ability to predict this effect." *Id*., 842. Together, in my opinion, Addy's experiments replicating the prior

art demonstrate that, even with an alcoholysis transesterification, a POSITA would not have expected OSI of transesterified products to necessarily increase relative to the feedstock. It is also worth noting that neither of these prior art documents in fact taught the use of a lipase to transesterify a wax ester rather than a triglyceride.

109. I note that in another experiment, Addy provided additional evidence of just how surprising and unexpected the results of the claimed invention were by comparing the results of a chemically-catalyzed ester-ester exchange and an lipase-catalyzed ester-ester exchange when feedstock contained 20% hydrogenated jojoba wax esters and 80% unsaturated jojoba oil. *See id.*, Pt 5, 1074-1079. The results showed that when a lipase was used, the OSI more than tripled (from 33.8 to 117 hours), compared to a statistically insignificant increase when a chemical catalyst was used (from 33.8 to 38 hours):

| Type | AV | PV | DP | Lovi | OSI | IV |
|---|---|---|---|---|---|---|
| Feedstock | 0.5 | 0.4 | N/A | 1.0R 3.4Y | 33.8 | 66.3 |
| Enzymatic | 0.19 | 0.9 | 48 | 0.9R, 2.9Y | 117 | 65.7 |
| Chemical | 0.04 | 0.2 | 47.3 | 0.3R, 1.3Y | 38 | 66.3 |

**Table 1 -- Physical Properties**

*Id*., 1076. Notably, the iodine values (IV) here were roughly the same for both transesterified products and the original feedstock, meaning that the chemical and enzymatic products contained roughly the same number of double bonds as the feedstock. *Id*. That the OSI increased without reducing the number of double bonds

in the product was surprising, and confirmed the data in the specification of the patent.

110. During an applicant-initiated interview, I understand that the Examiner ultimately found that these arguments were "persuasive because the declaration filed on 07/20/2021 shows that the enzymatic transesterification of jojoba oil feedstock with a lipase results in significantly higher OSI ***even without the addition of an alcohol***." *Id*., 1167 (emphasis added). The Examiner withdrew the pending obviousness rejection and the claims subsequently issued. In the Notice of Allowance, the Examiner specifically found the claims non-obvious over the prior art because of the unexpected result that increased OSI could be achieved without the addition of an alcohol :

> [T]he prior art is silent about the OSI of the transesterified product and teaches transesterification of the feedstock with a lipase with the addition of an alcohol to the feedstock. The instant method wherein a feedstock comprising jojoba wax esters and hydrogenated jojoba wax esters is enzymatically transesterified with a lipase ***results in an unexpected higher OSI of the transesterified product*** as compared to the OSI of the feedstock ***even without the addition of an alcohol***.

*Id*., 1178 (emphasis added). In other words, the Examiner found that it was unexpected that the OSI of the product could be higher than the OSI of the feedstock with the claimed lipase-based ester-ester exchange rather than an alcoholysis reaction.

## VII. PRIOR ART ANALYSIS

111. My findings, as explained below, are based on my study, experience, and background in the fields discussed below. I have also relied on my review and analysis of the prior art, information provided to me in connection with this case, and information I have independently reviewed.

### A. Ground 1 Fails to Disclose or Suggest the Claimed Invention

112. It is my opinion that Vantage's Ground 1 prior art fails to disclose (i) contacting a jojoba wax ester feedstock with a lipase, (ii) the OSI of the entire feedstock, (iii) increased OSI in the transesterified product compared to the feedstock, and (iv) the use of 20-50% hydrogenated wax ester in the feedstock. Ground 1 also fails to disclose the limitations of the dependent claims. I discuss each in turn.

#### 1. Neither Cummings, Xu, Nor Sessa Discloses "Contacting the [Jojoba Wax Ester] Feedstock with a Lipase"

113. Claim 1 requires "contacting the feedstock with a lipase," where the "feedstock" "compris[es] jojoba wax esters and hydrogenated jojoba wax esters[.]" Ex. 1001, cl. 1. I understand that Vantage does not dispute that neither Cummings nor Sessa discloses using a lipase to interesterify jojoba wax esters. Ex. 2046, 31:24-32:9, 59:17-19; Ex. 2047, 2. I understand that it is further undisputed that Xu provides no examples of using a lipase with jojoba wax esters. Ex. 2046, 56:10-57:19. Vantage instead argues that a "POSA would have found it obvious to modify

the catalyzed process of Cummings to use the lipase disclosed in Xu as the catalyst." Pet., 36. I disagree. Vantage does not cite any prior art that discloses or even suggests using a lipase to transesterify jojoba wax esters, nor have I been able to independently identify any such reference. Instead, all of the references Vantage relies upon, including Xu, only disclose transesterifying triglycerides.

114. As I discuss at length above, critical structural differences, namely jojoba wax esters' absence of a glycerol backbone, would have counseled a POSITA against using a lipase with jojoba wax esters. Despite these well-known differences, as well as the specificity of lipases for triglycerides, Vantage strangely never addresses why a POSITA would have expected a lipase-catalyzed ester-ester exchange to work on jojoba wax esters, which does not contain the structure that interacts with a lipase in triglycerides. In my opinion, this omission is consistent throughout Vantage's entire Petition, and undermines any obviousness argument.

#### *a. Vantage's Prior Art Only Discloses Lipase-Catalyzed Transesterification of Triglycerides*

115. In Ground 1, Vantage relies solely on Xu to disclose the use of a lipase to catalyze a transesterification reaction. But Xu does not teach or even suggest the use of a lipase with anything other than a glyceride-based molecule.

116. I note that Xu is a review article describing multiple ways in which lipase-based reactions have been utilized to modify the triglyceride structure. Xu describes, in a single section, the lipase-based ester-ester exchange in triglycerides

***only***. *See* Ex. 1008, 10-13. The reaction scheme Xu describes and illustrates in Figure 18 shows the ester-ester exchange of triglyceride chains using a *sn*-1,3 lipase:

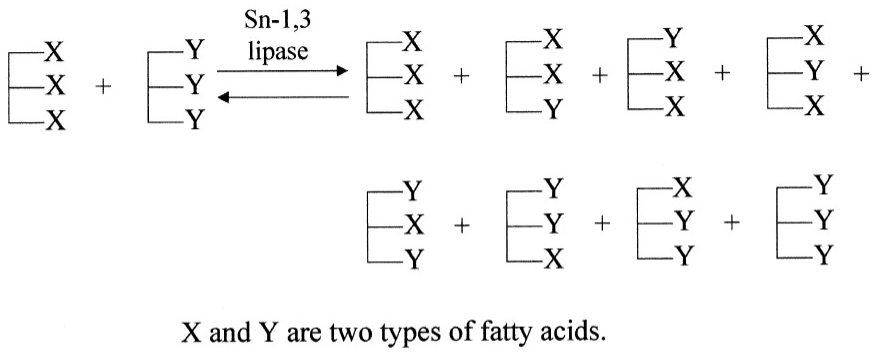


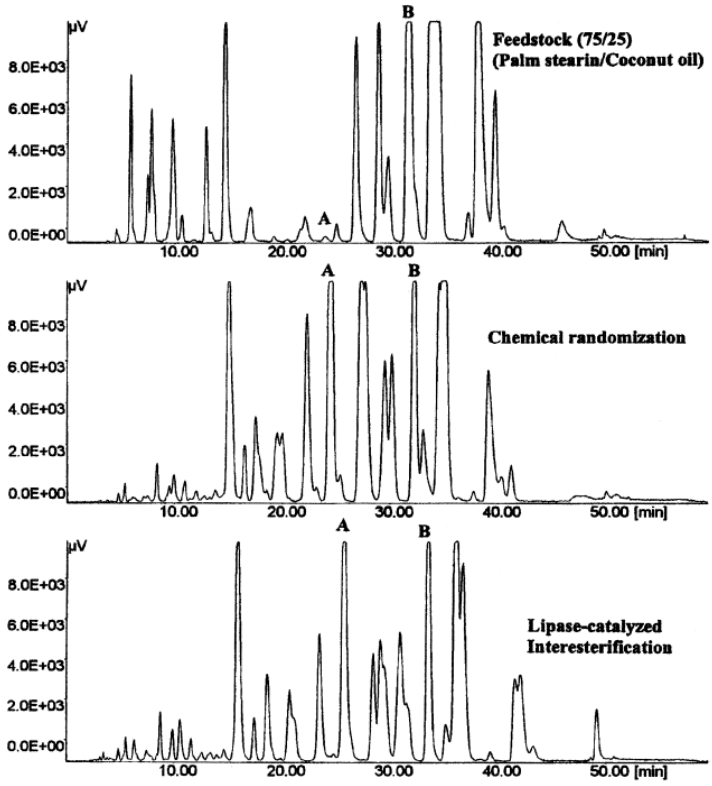

**Fig. 18.** Reaction scheme of enzymatic ester-ester exchange between two triacylglycerols (XXX and YYY) with *sn*-1,3 specific lipases.

Ex. 1008, Fig. 18.

117. I note that Xu describes in detail how lipases work on the specific triglyceride structure by exchanging *sn*-1,3 chains and maintaining the *sn*-2 chain. *Id*., 11; *see also id.* ("The equations for the calculation of different types of ***TAG*** [triacylglycerol] species are listed below"); *id.*, 12 ("The formed DAG [diacylglycerol] can esterify with another FFA [free fatty acid] ***to form a new TAG***"); *id.*, 13 ("Ester-ester exchange can also be used for the ***production of structured TAGs*** with the reaction between TAGs and fatty acid ethyl esters.") (emphasis added). In my opinion, a POSITA reading Xu would not find any explanation of how a lipase meant for use on a triglyceride could or would have been able to similarly act in an ester-ester exchange on a different structure lacking a

glycerol backbone, such as jojoba wax esters. As I describe above, a POSITA would have understood that lipases have high specificity in acting on triglyceride substrates. Ex. 2039, Abstract; Ex. 2028, 6. Nothing in Xu suggests that lipases could work on substrates like jojoba wax esters, which not only lack a triglyceride, but *any* form of a glycerol.

118. Additionally, in my opinion Xu shows that a POSITA would have actually expected ***different*** results when using a lipase catalyst to drive an ester-ester exchange. Xu's Figure 19 analyzes the results of chemically-catalyzed and lipase-catalyzed interesterification of a palm-oil derivative and coconut oil (both triglyceride compositions):



Ex. 1008, 11. Xu notes that the two interesterified products are "slightly different," and specifically notes two peaks that differ significantly, Peaks A and B. *Id.* In fact, Xu suggests that because Peaks A and B are "particularly different," they "can be used as markers" of the product's manufacturing process. *Id.* Therefore, not only would Xu's focus on triglycerides not have motivated a POSITA to try the same modifications with jojoba wax esters, but it also would have deterred a POSITA from replacing a chemical process, as lipases were shown to yield different products. Simply put, in my opinion there is no disclosure anywhere in Xu that would have motivated a POSITA to even consider utilizing a triglyceride-specific lipase to transesterify jojoba wax esters, let alone believe that it could be done successfully.

***b. Vantage Never Addresses the Structural Differences Between Triglycerides and Jojoba Oil***

119. Despite the well-known differences in chemical structures of triglycerides compared to jojoba wax esters, including the presence/absence of a glycerol backbone, positioning of the fatty acid chains relative to the ester, and number of the fatty acid chains, neither Vantage's Petition nor Dr. Rockstraw's Declaration acknowledged these differences or addressed the impact of these differences on lipase activity.

120. As I explained in detail above, jojoba wax esters have a long alcohol and a long acid chain extending to either side of a single ester group, as opposed to the three fatty acid chains coupled through three ester groups to a glycerol backbone

in a triglyceride. In my opinion, these conformational and dimensional differences are the key to why it was so unexpected for a lipase to interact with and, indeed, act upon, jojoba wax esters. *See* Section V(B)-(D). Unlike jojoba wax esters, the triglyceride's alcohol moiety is significantly smaller and has three separate -OH groups that can each be involved in an ester-ester exchange. Such structural differences would have been understood by a POSITA to hinder the jojoba wax ester's ability to move or position themselves to bind with the catalytic domain of the lipase binding sites. Ex. 2035, 2-3. A POSITA simply would not have expected a lipase to be able to bind to jojoba wax ester's single ester bond.

121. Although it was well known that lipases act on triglycerides with specificity, Vantage did not address why a POSITA would have understood Xu's disclosure of lipase catalyzation of ester-ester exchanges in triglycerides to be applicable to jojoba wax esters. In my opinion, a POSITA would have been aware of the specificity of lipase binding sites based on the size and shape of those binding sites, and would have further been aware of the differences in structures between triglycerides and jojoba wax esters. Ex. 2063, Fig. 1, 8-10. Furthermore, it is my opinion that it would not have been obvious to a POSITA that the lipase binding sites that were known to attach specifically to the glycerol backbone (i.e., the catalytic triad and oxyanion hole) at the start of an ester-ester exchange would work when exposed to molecules ***lacking*** that glycerol backbone. I note that Vantage

provided no prior art showing why a POSITA would have believed a triglyceride-specific lipase would work with jojoba wax esters, despite the jojoba wax esters missing these critical structural features.

122. I note that despite the fact that Xu was published a decade before the '245 patent and specifically stated that enzymatic transformation of triglycerides had been known for the previous 20 years, the only scientific data I have seen anywhere in the record (or in my independent review of the literature) showing the actual results of lipase-catalyzed transesterification of jojoba wax esters is in the specification and prosecution history of the '245 patent. I understand this to mean that for over 30 years no one knew that lipases could transesterify jojoba wax esters until the inventors of the '245 patent showed it. Given the structural differences between jojoba wax esters and triglycerides, in my opinion a POSITA simply would not have had a reasonable expectation that a lipase-catalyzed ester-ester exchange of jojoba wax esters would be successful, and therefore would not have been motivated to try it.

2. Cummings Does Not Disclose "OSI of the Feedstock"

123. Claim 1 requires a "feedstock" that "compris[es] jojoba wax esters and hydrogenated jojoba wax esters[.]" Ex. 1001, cl. 1. In my opinion, Vantage's Petition fails as to Cummings because Vantage does not (and, indeed, cannot) identify the claimed feedstock or the properties of that feedstock. As I understand

the Board correctly found, Cummings' "refined jojoba oil" forms only "part of" the feedstock, meaning the unsaturated part of the feedstock. I.D., 24 (citing Pet., 38). Vantage failed to identify where Cummings discloses an OSI value of a feedstock mixture containing both the saturated and unsaturated parts. *Id*. As such, I understand the Board found that "Petitioner does not identify clearly where Cummings discloses an OSI value of the fully saturated jojoba oil that forms the *other* part of the feedstock, much less the OSI of a feedstock mixture containing both the saturated and unsaturated parts." *Id*. (emphasis in original); *see also id.*, 28 ("[W]e are skeptical that Cummings alone discloses limitation 1[c][.]"). I believe the Board made the correct finding on this point.

124. Vantage relies on the statement in Cummings that "[j]ojoba esters demonstrate remarkable stability with OSI values of all jojoba esters greater than 100 hours and as high as 675 hours … [t]he OSI of refined jojoba oil is around 35 hours." Ex. 1004, 2; *see also* Pet., 38. But as the Board correctly noted, the refined jojoba oil is only one of the two required components of the claimed feedstock, and Vantage does not account for the contributions of both components of the feedstock (i.e., the jojoba wax esters and hydrogenated jojoba wax esters) to the OSI. Cummings describes OSI values for commercial jojoba ester products and refined jojoba oil but does not include an OSI value for a feedstock containing both jojoba wax esters and hydrogenated jojoba wax esters. Ex. 1004, 2.

125. I understand that Vantage may be alleging that the OSI of the feedstock is dictated solely by the OSI of the unsaturated jojoba wax esters, as Dr. Rockstraw stated on redirect at his deposition, (Ex. 2046, 139:23-141:16, 142:7-143:16), and is therefore 35 hours (i.e., the same as refined jojoba oil). Specifically, Dr. Rockstraw testified:

> Q. So the -- if I am understanding you correctly, you are saying that the OSI of a blend is dictated by the OSI of the unsaturated material?
>
> **A. Yeah. I think you call that "the weakest link." So, for instance, if I took -- the OSI device takes 5 grams of material, that's what the standard calls for you to put in it. If instead of 5 grams of refined oil, I put 4 grams of refined oil and 1 gram of fully hydrogenated wax in it, I would expect to get the same or similar result from that OSI. And in the intrinsic record I found evidence of that, so a person of skill in the art would recognize that, and it's confirmed or corroborated by the intrinsic record.**
>
> Q. And just to go a little bit further on that example; so if you had the 5 grams of material, if you put 4 grams of hydrogenated material and 1 gram of unhydrogenated, you would still expect to get similar OSIs?
>
> **A. I would. Your weakest link is still the oil, and I would expect that it may delay the onset a bit, but I would still expect it to be a similar result.**

Ex. 2046, 142:15-143:16.

126. I strongly disagree with this contention. I note that Vantage's Petition cites no evidence supporting that allegation, and this position is unsupported by the literature that I have reviewed. At a high level, I note that the method used to

measure OSI depends on the particular composition of the sample and the concentration of the materials being oxidized, i.e., on the number of double bonds present in the total mass of a given sample. Thus, it is the number of double bonds available for reaction with oxygen (relative to the total number bonds / or relative to the total composition) that influences the OSI. *See* Ex. 2002, 5 ("It is well known that the autoxidation of unsaturated fatty compounds proceeds at rates depending on the number and position of the double bonds."). When saturated wax esters are present in a mixture, the relative number of double bonds necessarily goes down, when compared against an equivalent amount of pure unsaturated jojoba wax esters. Therefore, the OSI value will increase, and Cummings does not disclose the new OSI value of that mixture.

127. At the outset, Dr. Rockstraw's position that the OSI of a feedstock is dictated solely by the unsaturated jojoba wax esters, or what he labels "the weakest link," is contradicted by Vantage's own references. For example, most of the Floraesters products described in Cummings and *Trans* Isomers 2 contain some amount of unsaturated jojoba wax esters. This is indicated in *Trans* Isomers 2, which shows that after transesterification, the transesterified product consists of a mix of fully saturated, partially saturated, ***and*** fully unsaturated wax esters. *See* Ex. 1006, 2; *see also* Ex. 1014, 6. Cummings also makes this point abundantly clear. In Figure 2 of Cummings, the composition of the specific esters is delineated for each of jojoba

oil, jojoba esters (15), jojoba esters (20), jojoba esters (30) & (60), and jojoba esters (70). Ex. 1004, 2. Notably, all of the jojoba esters apart from the fully saturated jojoba esters (70) product contain fully unsaturated wax esters, as evidence by the top 9 rows of the table, which all contain two double bonds, as demonstrated by the left most column. *Id*. If the OSI was determined based only on "the weakest link" of the unsaturated wax esters, then the OSI of all of the transesterified products containing fully unsaturated wax esters would be the same. But *Trans* Isomers 2 and Cummings show that is not the case. *See* Ex. 1006, 3; Ex. 1014, 7; Ex. 1004, 2; *see also* Ex. 2048, 15 (Floratech presentation demonstrating that jojoba esters 15 without tocopherols has OSI ~50 hours and jojoba esters 60 without tocopherols has OSI ~180 hours). Instead, OSI increases with increasing amounts of saturation, regardless of the presence of fully unsaturated wax esters. *Id*.

128. To the extent Dr. Rockstraw attempts to make this "weakest link" argument by using support from literature on triglycerides, in my opinion such a comparison is not supportable. As I have discussed at length above, the chemical properties of jojoba wax esters and triglycerides are distinct, and not interchangeable. I would expect differences between how triglycerides oxidize and how jojoba wax esters oxidize, in part because of the placement of the double bonds. In jojoba wax esters, there are at most only two double bonds on an ester, and they are separated by a long chain of carbons on either side of the ester bond. The double

bonds on a jojoba wax ester "are far apart and uneven from the center," in contrast to "typical plant oils," where double bonds are "usually close to each other." Ex. 2025, 9. The positioning of the double bonds can directly affect its oxidative stability. *See* Ex. 2002, 5 ("It is well known that the autoxidation of unsaturated fatty compounds proceeds at rates depending on the number ***and position*** of the double bonds.") (emphasis added). Therefore, in my opinion, it would be inappropriate to apply any assumption regarding oxidation of triglycerides to jojoba wax esters.

3. Vantage's Prior Art Does Not Disclose the Required Comparison of OSI Values

129. Claim 1 requires that "an oxidative stability index (OSI) of the transesterified product is greater than an OSI of the feedstock." Ex. 1001, cl. 1. Because Vantage's Petition does not identify an OSI value of a feedstock mixture in Cummings containing both saturated and unsaturated parts jojoba wax esters, the Board was unable to determine whether the asserted prior art in fact disclosed the comparison required by the claim between the OSI values of the product and the two-component feedstock.

130. Instead, the Board relied on three of Vantage's background references to support its conclusion that "through transesterification, the OSI of the resulting product could be improved" by "routine optimization[.]" I.D., 26. In my opinion, this argument fails because the Board did not fully appreciate that the claims do not

only require improved OSI in the product, but rather they require an improvement specifically *in comparison to the feedstock*.

131. I have reviewed these background references, and I note that each reference has the same deficiency as Cummings. None of the references include enough information to compare the OSI of the product to the OSI of the feedstock, let alone to conclude that the OSI of the product was higher than that of the feedstock. Vantage relies on the references' disclosures that allege the OSI of the product is higher than the unmodified oil to infer that the product OSI value is higher than that of the feedstock containing both the unmodified oil *and* the hydrogenated esters. But I see nothing in the record that supports that inference.

132. Saturated wax esters are well known to have high oxidative stability. *See, e.g.*, Ex. 1015, [0004] ("Saturated hydrocarbon based oils have no unsaturation and therefore have high oxidative stability."). In comparison, for instance, the Board found that Cummings disclosed that the refined jojoba oil forming the unsaturated part of the feedstock had an OSI value of "around 35 hours." I.D., 24 (citing Ex. 1004, 2). It is unknown based on the references what the oxidative stability would be of a feedstock containing 20-50% of fully hydrogenated wax esters, let alone whether transesterification would increase it even further. In my opinion, nothing that I see in Vantage's cited references or expert testimony fills this gap in proof. Furthermore, I note that Cummings reports only the OSI of the commercial ester

product which are further processed after transesterification (e.g., removal of transesterified alcohols and acids formed during chemical transesterification and addition of tocopherols).

133. I see that the Board cites Vantage's first background reference, Kodali, for the proposition that "[t]ransesterifying various short saturated fatty acid esters with vegetable oil *improves oxidative stability ... due to the increased saturation and the heterogeneity* of the fatty acid esters to the polyols." I.D., 26 (emphasis in original, citing Ex. 1015, [0005]). But the rest of that paragraph makes clear that the improved oxidative stability is in comparison to only the unmodified oil and does not factor in the saturated portion of the feedstock. *See* Ex. 1015 [0005] ("The invention is based on transesterifying … oils, such as vegetable oils, to obtain oils having improved lubrication properties."); *see also id.*, [0006] ("the invention features a method for improving lubrication properties of a vegetable oil."), [0025] ("A statistically significant improvement in lubrication properties is observed in comparison to a corresponding non-modified oil."). Additionally, I note that when interpreting Kodali's experimental results shown in Table 1, Kodali states that "[t]he oxidative stabilities of the transesterified products without added antioxidants ***were lower*** than the starting oil[.]" *Id*., [0081] (emphasis added). Table 1 shows the OSI of the IMC-130/TMPTH transesterified (TE) product is 17.90 hours, and the OSI of the IMC-130 "starting oil" is 38 hours. *Id*. The OSI of the feedstock—that is, the

IMC-130/TMPTH mixture ***before*** transesterification—is never given. *Id*. Thus, Kodali, which utilizes a chemical catalyst, is silent as to the oxidative stability of the feedstock, and in my opinion, no comparison can be made.

134. I see that the Board cites Vantage's second background reference, Xu 2, for the statement that this "[c]onfirm[s] that enzymatic interesterification has advantages for the oxidative stability of the products." I.D., 26 (citing Ex. 1017, 245). Here, the oxidative stability "advantages" Xu 2 describes are not in comparison to either the unmodified oil (here, "fat") or the feedstock, but rather in comparison to products "made from chemically interesterified fat," as opposed to enzymatically interesterified fat. Ex. 1017, 12. Therefore, like Kodali, Xu 2 is silent as to the oxidative stability of the feedstock. Indeed, it is silent as to the oxidative stability of any specific component in the process. Thus, in my opinion no conclusions can be drawn from Xu 2's statement in relation to the claimed comparison limitation.

135. I see that the Board cites Vantage's third background reference, Lopez-Hernandez, as "describing 'lipase-catalyzed interesterification' and noting the 'absence of unsaturated fatty acid residues implies that the products … have enhanced stability with regard to oxidation processes." I.D., 27 (citing Ex. 1018, C371). But this statement in Lopez-Hernandez is nothing more than a basic statement of chemistry. The reaction in Lopez-Hernandez is an ester-ester exchange

between two oils that both contain ***only*** saturated fatty acid residues. *See* Ex. 1018, 2. As I discuss above in Section V(B), when no unsaturated residues (i.e., double bonds) are present, a fatty acid is at its most stable. Therefore, Lopez-Hernandez's comment about the "absence of unsaturated fatty acids" causing enhanced stability is simply a factual statement about the saturated nature of the chosen oils. Lopez-Hernandez does not measure oxidative stability or OSI, and therefore no comparison of oxidative stability between the products and the feedstock can be made.

136. The Board also cites to two paragraphs from Dr. Rockstraw, to support its conclusion that the "totality of the argument and evidence cited by Petitioner is sufficient to meet the institution burden[.]" I.D., 27-28 (citing Ex. 1003, ¶¶122-123). But I have reviewed Dr. Rockstraw's declaration extensively, and in my opinion, Dr. Rockstraw does not fill the missing gap either. His paragraph 122 addresses the disclosures in Cummings that the Board found did not disclose 1[c]. Ex. 1003, ¶122. And paragraph 123 just repeats the same quotes from the prior art references I addressed above. *Id*., ¶123. Dr. Rockstraw, like Vantage and the Board, focused on the contention that transesterification "can produce a product having improved—and thus greater—oxidative stability," than the unmodified fat, oil, or wax ester. *Id*. Dr. Rockstraw never addresses whether the oxidative stability of the product is greater than the ***feedstock***.

137. Therefore, in my opinion, none of Vantage's prior art, whether used as a primary reference or as a background reference, support the finding that "it would have been obvious as a matter of routine optimization for a POSA to tailor the process to achieve" a transesterified product with OSI increased over the OSI of the feedstock. I.D., 26.

4. None of Vantage's Prior Art or Background References Discloses Increasing OSI of the Feedstock Through Transesterification

138. In addition to failing to provide evidence showing the required comparison between the product and the feedstock, in my opinion Vantage's Petition also fails because it does not explain why a POSITA would have expected OSI to ***increase*** in comparison to the feedstock after transesterification, as required by claim 1. *See* Ex. 1001, cl. 1. In fact, a POSITA would not have expected OSI to increase after transesterifying jojoba wax esters, because the number of double bonds—i.e., the source of oxidative ***in***stability—does not change in the claimed ester-ester exchange. None of Vantage's other references say otherwise. Thus, Vantage has not met its burden to show any comparison, let alone that the results of such a comparison reveal an increased OSI in the transesterified product.

***a. Cummings Does Not Show Transesterification Increases OSI Compared to the Feedstock***

139. In my opinion, nothing in Cummings suggests that the ***transesterification*** of refined jojoba oil, with nothing more, results in an increased

OSI of the Floraesters jojoba ester products. I observe that Cummings appears to be simply a marketing brochure for Floratech's Floraesters products[3], not a peer-reviewed publication showing statistically supported data. In contrast, the '245 patent demonstrates conclusively that chemical transesterification—that is, how the Floraesters products were formulated at the time of Cummings' publication—resulted in a product with ***lower*** OSI than the feedstock. Ex. 1001, 9:26-56. This finding is also consistent with other prior art such as Kodali, which disclosed decreased OSI after chemical transesterification and required the addition of antioxidants to bring the OSI of the product back up. Ex. 1015, [0081].

140. In my experience, a POSITA would instead have understood that ester products generally undergo additional processing after transesterification. Ex. 2064, 5. Specifically, with a jojoba wax ester, a POSITA would have understood that additional antioxidants (e.g., tocopherols) were likely to be added to increase OSI and enhance stability of the commercial product even further. It is the addition of

---

[3] I note that it was and is standard industry practice in these types of publications not to use trade names, which is why the products are identified as "Jojoba Ester" rather than "Floraesters" in Cummings. I further note that the first page of Cummings, however, does identify the Floraesters trade name. Ex. 1004, 1.

tocopherols that explains why the OSI of refined jojoba oil is reported as 35 hours but the OSI of Floratech's Jojoba Esters 15 commercial product, which has the same number of double bonds as refined jojoba oil, is nevertheless reported as 100 hours (Ex. 1004, 2) or 70 hours (Ex. 1006, 3), respectively. Indeed, I understand that Floratech's former Technical Director gave a 1998 presentation to the Society of Cosmetic Chemists, titled "Effects of Additives on the Oxidative Stability of Botanical Emollients," showing that the Floratech's Jojoba Esters 15 and Jojoba Esters 60 products referenced in Cummings and *Trans* Isomers 2 had added tocopherol. *Compare* Ex. 2048, 15 (Jojoba Esters 60 with tocopherol has OSI of ~225 hours; Jojoba Esters 15 with tocopherol has OSI of ~70 hours; Jojoba Esters 15 without tocopherol has OSI of ~35 hours), with Ex. 1006, 3 (Table 2).

141. I note that the addition of tocopherols is further supported by certificates of analysis for the Floraesters 20 and Floraesters 15 products from the time period of Cummings and *Trans* Isomers 2. *See* Ex. 2013, 1 (2004 certificate disclosing 0.05 wt% tocopherols in Floraesters 20); Ex. 2012, 1 (2004 certificate disclosing 0.05 wt% tocopherols in Floraesters 15); Ex. 2014, 2, 7 ([redacted]); Ex. 2049, 1, 2. Therefore, in my opinion, while a POSITA would have known that the commercial product has a higher OSI than refined jojoba oil, she would also have understood that the increase was attributable to the added tocopherol, and not to interesterification. The

disclosures in Cummings about the OSI of commercial products would not have led a POSITA to believe that simply transesterifying refined jojoba oil would result in an improved OSI, when no double bonds are being lost or gained.

### *b. A POSITA Would Not Have Expected OSI to Increase After Ester-Ester Exchange*

142. A POSITA would not have expected a meaningful change in oxidative stability of a transesterified product because the degree of saturation (i.e., the number of double bonds) does not change during ester-ester exchange.

143. The claims of the ’245 patent require “transesterifying the jojoba wax esters and the hydrogenated jojoba wax esters in the feedstock with the lipase to form a transesterified product.” Ex. 1001, cl. 1. Thus, I understand that the transesterification step recited in the claims of the ’245 patent is an ester-ester exchange, as opposed to an alcoholysis or acidolysis reaction. *See also* Ex. 2046, 23:2-12 (Dr. Rockstraw agreeing the claims are directed to ester-ester exchange). As I explain in detail above, jojoba oil (i.e., jojoba wax ester) is an unsaturated species that has two double bonds (one on each end of the molecule). Hydrogenated jojoba wax esters, on the other hand, are fully saturated and have zero double bonds. In an ester-ester exchange between these two compounds, the fatty chains on either side of their ester bonds are swapped, randomizing the chains found in the mixture, such that there will be a reduction in the amount of fully saturated wax esters (zero double bonds) and unsaturated wax esters (two double bonds) coupled with an

increase in the number of partially saturated wax esters (one double bond). Critically, the total number of double bonds in the mixture ***stays the same*** before and after the ester-ester exchange. Ex. 2046, 80:19-22 (Dr. Rockstraw agreeing the number of double bonds is the same in the feedstock and the product). As I explain above, the number of double bonds in a compound is a key predictor of oxidative stability. Because there is no net gain or loss in double bonds in the claimed transesterification process, in my opinion the POSITA would not have expected the oxidative stability to meaningfully change in the transesterified product.

144. I have seen other prior art references that confirm this. For instance, Rozenaal[4], a paper disclosing lipase-catalyzed ester-ester exchange of triglycerides, confirms my understanding that a POSITA would have expected no meaningful change in oxidative stability after an ester-ester exchange:

> Interesterification is one of three important fat modification processes. Unlike hydrogenation, it leaves the fatty acid composition unchanged and only alters the distribution of the fatty acids over the triacylglycerols. ***The stability of the oil remains essentially unchanged***, but important physicochemical properties such as melting, crystallization and recrystallization behavior are modified.

---

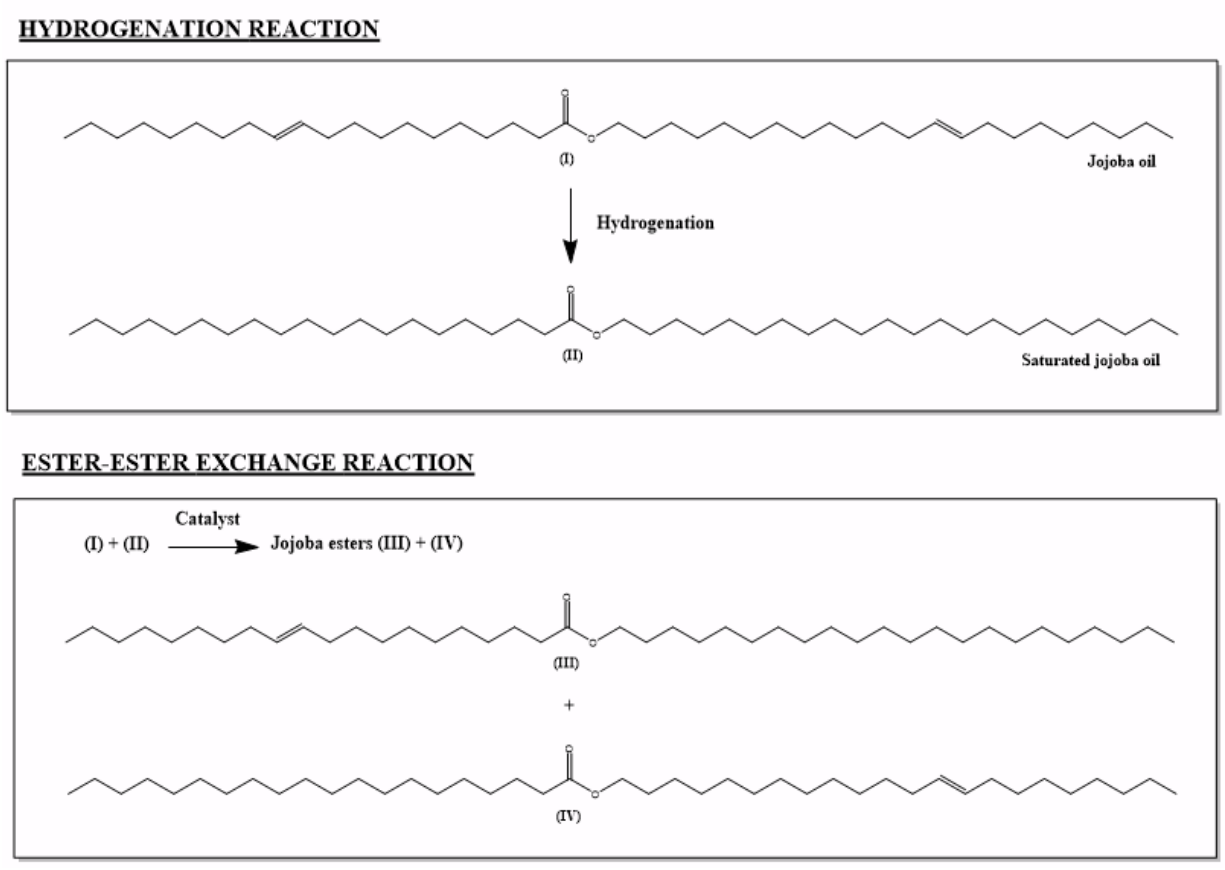
[4] I note that Rozenaal is the article that Vantage's Ground 3 prior art reference *Trans* Isomers 1 cites for the disclosure of using enzymes for interesterification. *See* Ex. 1005, 3.

Ex. 2030, 3 (emphasis added). Rozenaal explains that during an ester-ester exchange, "only" the distribution of the fatty acids is changed, with stability being "essentially unchanged." *Id*. In my opinion, Rozenaal's acknowledgement that oil stability remains "essentially unchanged" is an independent reflection of what was actually known in the art as of the Critical Date, and contradicts Dr. Rockstraw and Vantage's argument that a POSITA would have somehow expected an ester-ester exchange to increase the oxidative stability of the product over the feedstock. I note that Vantage has cited no prior art to the contrary.

145. In my opinion, the background references that Vantage and the Board rely upon to support the contention that it was known that OSI could be improved through transesterification all change the number of double bonds in the product. This shows that it was ***not*** the claimed transesterification that improved the OSI, but rather a reduction in the product's degree of saturation. For example, I note that the Board cited Kodali, stating that "[i]ndeed, Kodali discloses that '[t]ransesterifying various short saturated fatty acid esters with vegetable oil *improves oxidative stability…due to the increased saturation and the heterogeneity* of the fatty acid esters to the polyols.'" I.D., 26 (quoting Ex. 1015, [0005], emphasis in I.D.). Thus, in my opinion, Kodali is expressly connecting the observed improved oxidative stability to increased saturation, which, as I discuss above, simply does not happen when the process claimed in the '245 patent is used.

146. Likewise, I believe that the Board's statement that "***[m]odifying the saturation*** and heterogeneity within the resulting mixture of wax esters appears to be a key characteristic of the transesterification reaction itself," citing Figure 1 in Cummings (Ex. 1004), similarly overlooks that it is an ester-ester exchange being claimed. I.D., 26 (emphasis added). The Board's confusion in this respect is certainly understandable—Figure 1 of Cummings shows ***both*** hydrogenation, which saturates the two double bonds, ***and*** ester-ester exchange, which does not affect overall saturation. I have recreated and annotated the Cummings diagram below to make this point clear:

**Figure 1 - Jojoba ester production**



Adapted from Ex. 1004, 2. But as I explain above, hydrogenation and ester-ester exchange are ***two distinct*** steps. In the '245 patent, hydrogenation has already occurred, as the hydrogenated jojoba wax esters are part of the claimed feedstock that undergoes the ester-ester exchange. Ester-ester exchange itself does not affect the degree of saturation. So while the Board is correct that oxidative stability "depends in significant part on the degree of saturation," (I.D., 27) when the degree of saturation (i.e., number of double bonds) is not changed by the reaction, as is the case in the claimed method, a POSITA simply would not have expected the oxidative stability to change either.

147. In my opinion, the invention of the '245 patent is not obvious in part because it was so surprising that a meaningful increase in OSI could be achieved with the same number of double bonds present in both the feedstock and the transesterified product.

5. Vantage's Use of Iodine Values to Back-Calculate Percent of Hydrogenated Wax Esters in the Feedstock Was Unreliable

148. Claim 1 requires a feedstock "wherein the amount of hydrogenated jojoba wax esters is 20% to 50% by weight of the feedstock." Ex. 1001, cl. 1. In Ground 1, the Petition concedes that "Cummings does not expressly disclose '20% to 50%' in specific words[.]" Pet., 29 (emphasis omitted). Indeed, Cummings does not provide ***any*** description of the weight percentages of reactants contained in a feedstock used in producing the various commercial jojoba esters described in Fig.

3. Accordingly, Cummings does not disclose the claimed feedstock in which an "amount of hydrogenated jojoba wax esters is 20% to 50% by weight."

149. Instead, Vantage attempted to estimate the weight percentage of the reactants in the feedstock based on an alleged correlation between an iodine value ("IV") given in the prior art and the number of double bonds present in the product. Pet., 29-31. As the Board correctly recognized, this attempt fails for multiple reasons. *See* I.D., 18-19.

152. Vantage fails to establish what the actual compositions of the jojoba esters "products" are and therefore cannot correlate the products' iodine value to its feedstock. The iodine values reported by Cummings are associated with commercial jojoba ester products following transesterification. *See* Ex. 1004, Fig. 3. Back-calculation of the weight percentages of the original feedstock components (i.e., the reactants) from this value mistakenly relies on multiple assumptions about the products and the compounds that might form the feedstocks from which the products are formed.

153. Iodine value is not intended to provide information about the contents of a feedstock from which a product is formed – it is most commonly used to monitor the progress of a reaction. Iodine value is a measure of total saturation or unsaturation of an oil or fat. *See* Ex. 2002, 1, 2. "IV has been included in the standards of some industrial products derived from vegetable oils and fats, such as

biodiesel [and i]t is also occasionally used in assessing oxidative stability of oils and fats and their derivatives[.]" *Id.*, 1. The theoretical iodine value of a pure compound can be calculated based on the molecular weight of the compound and the number of double bonds present in the compound (because the iodine atoms are added to each double bond in the wet chemical method for determining IV). *Id.*, 2.

154. Cummings does not describe the transesterification processing methods used to produce the jojoba esters and corresponding yields, and, as a result, it is not possible to assess whether the products are reflective of actual reaction products of a transesterification process. For example, does "Jojoba esters (30)" reflect a product that contains only desired ester compositions as shown in Fig. 2 of Cummings? Or does "Jojoba esters (30)" also include side-products or unreacted feedstock, as might be expected in a chemical transesterification process? Or is "Jojoba esters (30)" subjected to post-reaction refining processes that further purify the esters contained in the "product"? Any of these or other scenarios related to the contents of the Jojoba esters product could impact the iodine value of the "Jojoba esters (30)" product by changing the binding of the iodine to the double bonds or providing additional products that interact with the iodine, for example. As I discuss above, a POSITA would have understood that the commercial products generally undergo additional processing before being sold, with various additives put into the product. Indeed, I note that the Floratech certificates of analyses and manufacturing

protocol bears this out, showing that tocopherols, for example, were added to the final Floraesters products—the very products whose OSI values are referenced in Cummings. *See* Section VII(A)(4)(a); Ex. 2012; Ex. 2013; Ex. 2014.

155. Accordingly, any of these scenarios could impact the estimated weight percent of the reactants estimated by the back-calculation. Multiple questions exist, the answers to which are highly relevant to the back-calculation proposed by the Petition, and these questions are unanswered by Vantage. Because the answers to these questions about the contents of the product would significantly affect whether one can establish any conclusions about the reaction product, as well as its reactants (e.g., feedstock), Vantage's back-calculation of weight percentages of the reactants based on the iodine value of the "product" cannot be relied upon. *See* Ex. 2002, 1 ("structure indices [such as iodine value] of fatty compounds can be influenced by the presence of accompanying materials…. as these indices often depend on the amounts of all components of a mixture."). Because the Petition fails to establish what the full composition of each jojoba ester product listed in Figure 3 is, it is not possible to know the weight percentages of the reactants based on the product's iodine values.

156. Finally, the Vantage's back-calculation neglects to consider the impact of other factors on the iodine value of a product. "The IV of higher esters decrease with increasing size of the alcohol moiety [as a] result of the IV being dependent on

the M.W. [molecular weight] of the fatty compound." Ex. 2002, 2. While the iodine value of a pure compound may be calculated based on knowledge of the molecular weight and the number of double bonds present, back-calculation of the reactants from an iodine value of a product is not so straight-forward as Vantage makes out.

157. "[A] given IV can be satisfied by different FA [fatty acid] profiles[.]" Ex. 2002, 3. This is a result of the IV of a mixture of fatty compounds being dependent on the amounts of the fatty components of the mixture "but not on the exact nature of the double bonds in the structure of those fatty compounds[.]" *Id.* A given iodine value can be reached by multiple compositions of a set of fatty acids, and by multiple combinations of various fatty acids. This, along with the lack of information about the products themselves, makes the estimation of weight percentages of the reactants by back-calculation from IV imprecise at best. *See also* Ex. 2002, 2 ("Many wet chemical methods for determining IV and SV have limited applicability and/or are error-prone as stated in remarks that accompany these methods.").

158. Vantage fails to address the actual compositions of the jojoba ester products relative to the reactants, and instead relies on a method of back-calculation to estimate the weight percent of the reactants without accounting for the assumptions underlying the use of iodine value in this estimation. This reliance on

the back-calculation to determine the weight percent of the reactants is inaccurate and, in my opinion, is based on untenable assumptions.

159. Apart from the iodine value calculations, I note that Vantage also relies on Sessa to teach the limitation of "wherein the amount of hydrogenated jojoba wax esters is 20% to 50% by weight of the feedstock." Pet., 31-35. Sessa teaches testing the properties of a range of Floraesters final products (i.e., calibration sets) made with a chemical catalyst and subject to further processing. Ex. 1009, 1-2. But Sessa's calibration sets do not meet this limitation, because Sessa does not disclose a ***feedstock***. I note that Sessa's "Materials and Methods" section is a single sentence that states: "[n]atural cocoa butter and the calibration sets consisting of native jojoba wax esters that ***were transesterified*** with proportionate blends of completely hydrogenated wax esters ***to give*** a series of 50, 100, 150, 200, 300, 400 and 500 g $kg^{-1}$ saturated ester ***were provided*** by [Floratech]." *Id*., 2 (emphasis added); *see also id.*, 4 (thanking Floratech "for supplying jojoba wax ester calibration set"). In other words, Sessa uses products that have already been transesterified and further processed. The feedstock Floratech used to perform the transesterification and processing to make those transesterified products is not disclosed. Therefore, Sessa is just as silent to the composition of the feedstock as is Cummings. Consequently, Vantage has no evidence to support its contentions regarding limitation [1a] requiring 20-50% by weight hydrogenated jojoba wax esters in the feedstock.

6. Dependent Claims Are Patentable Over Ground 1 Prior Art

160. I note that Vantage's Petition gives short-shrift to dependent claims 2, 3, and 5. Claim 2 requires that the feedstock "consists essentially of the jojoba wax esters and the hydrogenated jojoba wax esters," meaning that it does not contain other materials in the feedstock that could alter OSI. Ex. 1001, cl. 2. Vantage argues that the same combination that renders claim 1 unpatentable "teaches such a feedstock—*e.g.*, no additional OSI-affecting materials," and therefore meets claim 2. Pet., 41. Vantage makes no other effort to show how the feedstocks in Cummings or Sessa meet this limitation. Vantage instead relies on the scantness of their disclosures to meet this limitation. But neither Cummings nor Sessa discloses the full composition of the feedstocks to know whether they in fact contain any additional OSI-affecting materials. Sessa's "Materials and Methods" section is a single sentence that explains Sessa used an already-transesterified product, with no detail of how that was done or what feedstock was used. Ex. 1009, 2. Likewise, other than identifying the individual fatty acids found in the jojoba esters, Cummings does not disclose any other information about the composition of those commercial products, let alone their feedstocks. *See* Ex. 1004, 2. This lack of information is not sufficient to disclose this limitation.

161. Claims 3 and 5 require that the feedstock does not comprise "any free fatty alcohols" or "any methyl esters," respectively. Ex. 1001, cls. 3, 5. Because

neither Cummings nor Sessa discloses any information about the composition of the feedstocks used to produce their transesterified products, these limitations have not been shown in the prior art.

### B. Ground 2 Fails to Disclose or Suggest the Claimed Invention

162. It is my opinion that Vantage's Ground 2 prior art, like its Ground 1 prior art, fails to disclose (i) contacting a jojoba wax ester feedstock with a lipase, (ii) the OSI of the entire feedstock, (iii) increased OSI in the transesterified product compared to the feedstock, and (iv) the use of 20-50% hydrogenated wax ester in the feedstock. Ground 2 also similarly fails to disclose the limitations of the dependent claims.

#### 1. A POSITA Would Not Have Been Motivated to Use Xu's Lipases with *Trans* Isomers 2

163. Relying on *Trans* Isomers 2 instead of Cummings does not rectify Ground 1's lack of disclosure of lipases for esterification, as *Trans* Isomers 2 is also silent as to lipases. For the same reasons I discuss above in Section VII(A)(1) for Ground 1, a POSITA reading Xu would not have been motivated to use a lipase with *Trans* Isomers 2 or have expected transesterification with lipases to result in increased OSI compared to a feedstock.

#### 2. Vantage Fails to Identify OSI Values in *Trans* Isomers 2

164. *Trans* Isomers 2 has similar disclosures to Cummings, reporting the OSI values for Jojoba Esters 15, 20, 30, 60, and 70 in Table 4. *See* Ex. 1006, 3.

Again, as with Cummings, these values are for the OSI of Floratech's Floraesters products that have undergone post-transesterification processing including addition of tocopherols, as I discuss above for Ground 1.

165. Vantage relies on *Trans* Isomers 2's description of a partially hydrogenated jojoba oil as the alleged feedstock, but as the Board correctly noted, there is "no teaching in Trans Isomers 2 that the 'Jojoba oil Partial Hydrogenate[s]' of Table 4 form any part of a feedstock," rather "[t]o the contrary, these hydrogenates appear to be comparative *products* made by a different method—not interesterification." I.D., 33. The Board also correctly noted that the fact that these "Partial Hydrogenate[s]" include a material *trans* isomer component, when the same document states that the "reported Jojoba Esters contain ***no*** trans isomers only underscores that Table 4's hydrogenates are neither the feedstock nor the product of interesterification." *Id*. (emphasis in original).

166. Because *Trans* Isomers 2 does not disclose the OSI of a feedstock, in my opinion it clearly is unable to disclose a comparison between the OSI of a feedstock and a transesterified product, let alone whether OSI increased or decreased.

3. Iodine Values Cannot Be Used to Calculate Percent Hydrogenated Feedstock

167. In my opinion, relying on *Trans* Isomers 2 instead of Cummings does not rectify Ground 2's unreliable iodine value calculations, for the same reasons that I explained above in Section VII(A)(5) with Ground 1.

4. Dependent Claims Are Patentable

168. Relying on *Trans* Isomers 2 instead of Cummings does not rectify Ground 2's deficiencies as to claims 2, 3, and 5, because *Trans* Isomers 2 identifies the same transesterified products as Cummings, with no additional details about the feedstock used to produce those products. Therefore, claims 2, 3, and 5 are patentable for the same reasons that I explained above in Section VII(A)(6) with Ground 1.

### C. Ground 3 Fails to Disclose or Suggest the Claimed Invention

169. It is my opinion that Vantage's Ground 3 prior art, like its Ground 1 and 2 prior art, fails to disclose (i) contacting a jojoba wax ester feedstock with a lipase, (ii) the OSI of the entire feedstock, (iii) increased OSI in the transesterified product compared to the feedstock, and (iv) the use of 20-50% hydrogenated wax ester in the feedstock. Ground 3 also similarly fails to disclose the limitations of the dependent claims.

1. A POSITA Would Not Have Been Motivated to Use *Trans* Isomers 1's Enzymes with *Trans* Isomers 2

170. In my opinion, relying on *Trans* Isomers 1 instead of Xu does not rectify Ground 1 or 2's lack of disclosure of lipases for esterification, as *Trans* Isomers 1 contains an even more sparse disclosure of lipases than does Xu.

171. I note that Vantage relies on a single sentence from *Trans* Isomers 1 under the heading "Alternatives to Trans Isomers in Cosmetic Products" that does not mention jojoba wax esters, and merely states "Rozenaal [8] discussed use of this interesterification process to modify the melting characteristics of triglycerides using various catalysts including enzymes." Ex. 1005, 3. This sentence discloses nothing more than the possibility of selecting an enzyme catalyst amongst other "various catalysts" to interesterify triglycerides as a means of changing its melting characteristics. *Id*. Indeed, Rozenaal itself confirms this. *See* Ex. 2030, 3 ("Unlike hydrogenation, it leaves the fatty acid composition unchanged and only alters the distribution of the fatty acids over the ***triacylglycerols***."); *id*. ("Interesterification will lead to the so-called random distribution of fatty acids over the ***triacylglycerols*** if the process is carried out in a single phase with the usual types of catalysts."), ("Enzymes, such as lipases, can accomplish the exchange of fatty acids at the external positions of the triacylglycerol molecule but leave the fatty acid composition at the 2-position unchanged"); *id*., 4 ("In Table 1 the number and amount of the various ***triacylglycerols*** obtainable by interesterfication of a mixture

containing different fatty acids are shown.") (emphasis added). Nothing in Rozenaal teaches or suggests the transesterification of jojoba wax esters or any other wax ester, let alone the use of a lipase to catalyze the transesterification of jojoba wax esters.

172. Therefore, for the same reasons I discussed above for Ground 1 in Section VII(A)(1), a POSITA reading *Trans* Isomers 1 would not have been motivated to use a lipase with *Trans* Isomers 2 or have expected esterification with lipases to result in increased OSI compared to a feedstock.

2. Vantage Fails to Identify OSI Values in *Trans* Isomers 2

173. Relying on *Trans* Isomers 1 instead of Xu does not rectify Ground 1 or 2's lack of disclosure of a comparison showing increased OSI of an esterified product compared to the feedstock, since *Trans* Isomers 1, like Xu, does not disclose OSI values. Ex. 2046, 33:6-15.

3. Iodine Values Cannot Be Used to Calculate Percent Hydrogenated Feedstock

174. Relying on *Trans* Isomers 1 instead of Xu does not rectify Ground 3's unreliable iodine value calculations, for the same reasons that I explained above in Section VII(A)(5) with Ground 1.

4. Dependent Claims Are Patentable

175. In my opinion, relying on *Trans* Isomers 1 instead of Xu does not rectify Ground 3's deficiencies as to claims 2, 3, and 5, for the same reasons as discussed with Grounds 1 and 2.

### D. Ground 4 Fails to Disclose or Suggest the Claimed Invention

#### 1. A POSITA Would Not Have Been Motivated to Use Xu's Lipases with Brown

176. In my opinion, relying on Brown in addition to Cummings does not rectify Ground 1's lack of disclosure of lipases for esterification, as Brown is similarly silent as to lipases. *See* Ex. 2046, 50:17-52:3. For the same reasons that I discuss above in Section VII(A)(1) for Ground 1, a POSITA reading Xu would not have been motivated to use a lipase with either Brown or Cummings, or have expected esterification with lipases to result in increased OSI compared to a feedstock.

#### 2. Vantage Fails to Identify OSI Values in Brown

177. Relying on Brown in addition to Cummings does not rectify Ground 1's lack of disclosure of the OSI of a feedstock or a comparison showing increased OSI of an esterified product compared to the feedstock, since Brown does not disclose OSI values. Ex. 2046, 52:4-14. Additionally, I note that Brown primarily discloses an alcoholysis reaction, not an ester-ester exchange as required by the claims, rendering it even further inapposite. *See* Ex. 1007, 3:59-4:3.

#### 3. Iodine Values Cannot Be Used to Calculate Percent Hydrogenated Feedstock

178. Relying on Brown in addition to Cummings does not rectify Ground 1's unreliable iodine value calculations, for the same reasons that I explained above in Section VII(A)(5) with Ground 1.

4. Dependent Claims Are Patentable

179. In my opinion, relying on Brown in addition to Cummings does not rectify Ground 1's deficiencies as to claims 2, 3, and 5. Regarding claim 2, Brown is silent as to other ingredients that may affect OSI; Brown does not teach that such ingredients should be excluded from the feedstock. Regarding claim 3, free fatty alcohols are alcohols that contain long carbon chains (between 4 and 26 carbons) and are not attached to an ester. Brown expressly discloses using such free fatty alcohols in the "[s]tarting materials" or feedstock. *See* Ex. 1007, 4:7-18 (disclosing starting material of $R^4$-OH, then defining $R^4$ as "an alkyl group or other aliphatic group, preferably of 1 to 12 carbon atoms[.]"); *id.*, 4:63-64 (same). Regarding claim 5, Brown is also silent as to methyl esters; Brown does not teach that methyl esters should be excluded from the feedstock. Therefore, claims 2, 3, and 5 are patentable.

## E. Secondary Considerations of Non-Obviousness

180. In my opinion, the novelty of using the '245 patent's lipase-catalyzed ester-ester exchange process to transesterify jojoba wax esters is further demonstrated by significant evidence of secondary considerations of non-obviousness, including unexpected results.

181. Vantage's Petition and the Board's Institution Decision rely on the assumption that a transesterification reaction inherently results in a product with increased oxidative stability or OSI. Pet., 38-40; I.D., 26. But the prior art, the

specification of the ’245 patent, and the testing disclosed during prosecution demonstrate that this assumption does not hold true, for either chemical or enzymatic transesterification.

182. Regarding chemical transesterification, as I noted previously above, the Board relies heavily on Kodali’s allegation that “[t]ransesterifying various short saturated fatty acid esters with vegetable oil *improves oxidative stability*[.]” I.D., 26 (quoting Ex. 1015, [0005], emphasis in I.D.). In addition to being inapposite for the reasons I explained above, in my opinion this generalized statement is also undermined by Kodali’s own experimental results. In Example 5, Kodali provided data for its transesterification method, and observed from Table 1 that “[t]he oxidative stabilities of the transesterified products without added antioxidants ***were lower*** than the starting oil[.]” Ex. 1015, [0081] (emphasis added). I note that in order to achieve an oxidative stability that was greater than the oxidative stability of the feedstock, antioxidants had to be added. *Id*.

183. Further, in my opinion the statements in Kodali are consistent with the ’245 patent’s description of prior art chemically catalyzed processes that resulted in products with lower OSI than the unmodified oil and the ’245 patent’s testing using a chemical catalyst. *See* Ex. 1001, 7:24-42, 9:26-47. In contrast, as discussed above in Section III(A), in the claimed invention using a lipase catalyst, the oxidative stability surprisingly improved without the addition of ***any*** antioxidants. *Id*., 9:26-

47. Further, the ’245 patent notes that the improvement in oxidative stability could not be explained simply by the preservation of the tocopherols naturally present in the jojoba wax esters. *Id*., 9:56-62. Therefore, in my view, the data in Kodali independently confirms that a POSITA as of the Critical Date would have understood that obtaining a product with higher OSI was not a matter of simply transesterifying a feedstock.

184. Regarding enzymatic transesterification, in addition to the surprising results disclosed in the ’245 patent that I discuss at length in Section VI(A), the two declarations submitted during prosecution from inventor Jeff Addy demonstrated that different, and sometimes even opposite results could be obtained using the same transesterification reactions—here, prior art alcoholysis methods. As I discussed in Section VI(C), Addy first replicated a lipase-catalyzed alcoholysis reaction from Steinke using two oils that had similar starting oxidative parameters: a triglyceride oil (crambe oil) and jojoba oil (i.e., jojoba wax esters). Far from obtaining the same result, I see that Addy found that enzymatic alcoholysis had a negligible effect on crambe oil, with an increase of only about one hour, but effected over a three-fold increase in oxidative stability of jojoba oil. Ex. 1002, Pt. 2, 467-468. Addy then replicated a different alcoholysis method from Gunawan, comparing the effects of transesterifying another triglyceride oil (sunflower oil) as compared to jojoba oil. This time, the alcoholysis reaction had the opposite effect—the oxidative stability

of the transesterified jojoba oil went down compared to the feedstock, while the oxidative stability of the transesterified sunflower oil increased slightly. *Id*. Pt. 4, 841.

185. In my opinion, Kodali and Addy's testing support the '245 patent's disclosure of the unpredictable nature of transesterification reactions and the unexpected results achievable with the claimed invention. It was therefore surprising that the claimed invention of a lipase-catalyzed ester-ester exchange could in fact increase the OSI of the transesterified jojoba wax ester product in comparison to the feedstock.

## VIII. CONCLUSION

186. I reserve the right to supplement my opinions to address any information obtained, or positions taken, based on any new information introduced throughout this proceeding.

187. I declare under penalty of perjury that the foregoing is true and accurate to the best of my ability.