IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:	SAMPALIS, Fotini	Confirmation No.:	1767
Serial No.:	13/189,714	Group Art Unit:	1629
Filed:	July 25, 2011	Examiner:	POLANSKY, Gregg

FOR: **NATURAL MARINE SOURCE PHOSPHOLIPIDS COMPRISING POLYUNSATURATED FATTY ACIDS AND THEIR APPLICATIONS**

Mail Stop Declaration
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF JACEK JACZYNSKI, PH.D. UNDER 37 C.F.R. § 1.132

I, Jacek Jaczynski, declare as follows:

1. I am a tenured Associate Professor of Food Science and Technology at West Virginia University; Davis College of Agriculture, Natural Resources, and Design; Division of Animal and Nutritional Sciences. My appointment is 50% research and 50% teaching. I have been a professor at West Virginia University since 2002.

2. I earned a Ph.D. in Food Science and Technology in 2002 from Oregon State University, Seafood Research and Education Center. Immediately following my doctoral work, I joined West Virginia University as a faculty member. For the past 14 years I have been actively pursuing scientific research specializing in aquatic foods, with an emphasis on krill. I have published 15 book chapters and over 50 peer-reviewed articles on food science and technology, many in high impact journals as indexed by Journal Citation Reports.® For example, one of my peer-reviewed publications directly concerns solvent extraction of krill

oil.[1] In addition, I am the sole inventor of an issued patent (U.S. 7,763,717) and the inventor of two other patent applications currently under examination. One focus of my patent and patent applications is a method for isolating lipids from krill.

3. I serve on the Editorial Board for the *Journal of Aquatic Food Product Technology* and as a peer-reviewer for several food science journals, such as *Food Chemistry* and the *Journal of Agricultural and Food Chemistry*. I am a professional member of the Institute of Food Technologists ("IFT"), the American Chemical Society, the World Aquaculture Society, and Gamma Sigma Delta, an honorary society of agricultural scientists. I served as a Chair of the Division of Aquatic Food Products of the IFT for the 2010-2011 term. For the past 10 years I have also taught food science-related courses at West Virginia University, many of which enroll over 300 students annually. My curriculum vitae is attached as **Appendix A**.

4. In December of 2011, I was engaged by counsel for Neptune Technologies and Bioressources, Inc. ("Neptune") to review U.S. Patent 8,030,348 ("the '348 patent") and its substantive prosecution history, the Corrected Request for Reexamination filed by Aker Biomarine ("Aker"), listed as U.S.S.N. 95/001,714, including the Declaration of Mr. Bjorn Ole Haugsgjerd and the Declaration of Dr. Thomas Gundersen, and supporting materials, and to provide my expert scientific opinion regarding whether Gundersen and Haugsgjerd accurately followed the process disclosed in patent publication WO 00/23546 ("Beaudoin I") and CA 2,251,265 ("Beaudoin II") and therefore whether the data presented by Aker accurately characterized the krill extract obtained by Beaudoin. Also, I was asked to express my opinion on why intact phospholipids bearing omega 3 fatty acids, such as those found in krill oil extracts, are superior to other forms of omega 3 fatty acids, such as the triglyceride-bound forms seen in fish and algal oils, as well as free fatty acids.

5. I have had no prior direct involvement with either Neptune or Aker. I am being compensated at my customary hourly rate for my time spent on developing, forming, and expressing the facts and opinions in this declaration. I have no personal interest in the ultimate outcome of

[1] *See* Gigliotti *et al.* "Extraction and Characterisation of Lipids from Antarctic Krill (*Euphausia superba*)" *Food Chemistry* 125(3): 1028-1036 (April, 2011), **Appendix B**.

the reexamination proceedings involving the '348 patent or any continuation applications derived from the '348 patent.

6. I have carefully read the information provided and also conducted my own search of relevant, peer-reviewed scientific literature. Below I provide my expert scientific opinion.

Gundersen and Haugsgjerd Did Not Accurately Replicate Beaudoin I or Beaudoin II.

7. In my opinion, Gundersen and Haugsgjerd did not accurately reproduce the methodology for total lipid extraction from krill that is disclosed in Beaudoin I or II. Specifically, Gundersen did not sufficiently heat the krill oil samples in a manner that was appropriate to replicate Beaudoin I or II, and Haugsgjerd did not accurately replicate the extraction method of Beaudoin I or II because he added a significant step to the Beaudoin protocol. For at least these reasons, it is my opinion that Haugsgjerd and Gundersen failed to opine on the specific process of Beaudoin I or II and therefore failed to characterize the krill extract actually produced by Beaudoin I or II.

Gundersen Did Not Appropriately Heat the Samples.

8. Gundersen conducted the last step of the krill oil extraction procedure (which was partially conducted by Haugsgjerd). In doing so, Gundersen applied heat in a manner inconsistent with Beaudoin I or II to the krill oil extracted by Haugsgjerd. Specifically, Gundersen alleges that he conducted a heat treatment at 125°C for 15 minutes or at 70°C for 5 minutes, in an attempt to reproduce Beaudoin I and II (*see* Gundersen Declaration, Exhibit 2, Analytical Report second of two pages numbered 1, between page 5 and page 7).[2] However, in his attempt to heat the oil, Gundersen placed a heat block inside the oven of a gas chromatograph set to either 70°C or 125°C for at least one hour (*see* Gundersen Declaration, Analytical Report second page numbered 1, between page 5 and page 7). A vial of krill oil extract was then heated using the heat block for 15 minutes at 125°C or 5 minutes at 70°C (*see* Gundersen Declaration, Exhibit 2, Analytical Report second of two pages numbered 1, between page 5 and page 7). After Gundersen heated the vials, they were allowed to cool on

[2] I respectfully note that the confusion regarding page numbers in the Gundersen declaration stems from the declaration apparently being submitted either out of order or with incorrect pagination.

a laboratory bench to room temperature (*see* Gundersen Declaration, Exhibit 2, Analytical Report second of two pages numbered 1, between page 5 and page 7).

9. In my opinion, this heat treatment did not allow the oil to be heated to the temperature disclosed by Beaudoin I or II for the time specified by Beaudoin I or II due to slow heat transfer to the oil from the heat block. Gundersen's heating method was mediated primarily by air-liquid convection and not conduction. It is a well-established fact that conduction results in much quicker heat transfer than convection.[3] In simple terms, heated air contains relatively fewer molecules that can transfer heat from one object to another, as compared to heated liquids, such as oils as in a heated oil bath. Therefore, the transfer of heat via convection is much slower than conduction; thus, the samples heated as described by Gundersen were not maintained at the temperature of 125°C for 15 minutes or 70°C for 5 minutes.

10. A simple analogy allows illustration of this complex phenomenon. Consider placing one's hand in a standard kitchen oven set at a moderate temperature, say 400°F (which is about 200°C). One could easily hold one's hand in this oven for a period of time before experiencing physical discomfort or injury. If one were to place one's hand in a pot of boiling water (*i.e.*, around 100°C), however, one would immediately experience a burning sensation. This common scenario is explained by the difference between heat transfer by a slower method, convection (*i.e.*, the stove in the analogy), versus a faster method, conduction (*i.e.*, the boiling pot of water in the analogy).

11. Accordingly, when Dr. Gundersen placed the extracted krill oil in a heat block, he relied on heat transfer by convection to allegedly heat the oil to 125°C (or 70°C). Like the hand in the oven described above, the oil samples themselves did not reach and maintain a temperature of 125°C for 15 minutes. In contrast, during the prosecution of U.S. Patent 8,030,348, the applicant submitted data obtained after heating for 15 minutes at 125°C by placing the

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[3] *See, e.g.*, Singh and Heldman, *Introduction to Food Engineering* (3rd ed.), New York, NY: Academic Press, 2008 (pp. 222-27), **Appendix C**; Heldman and Lund, *Handbook of Food Engineering*, New York, NY: Marcel Dekker, 1992 (pp. 247-59), **Appendix D**, both of which are fundamental food engineering textbooks.

extracted oil in an oil bath, which, in my opinion, accurately re-created Beaudoin I.[4] Using this appropriate heat transfer method, mediated by conduction, the oil reached 125°C and therefore experienced a full 15 minute exposure to this temperature.

12. I also note that the proper use of a heat block to heat an oil extract effectively has been described in the literature. For example, in Herman and Groves,[5] the authors conduct an experiment in which they thermally stress lipid emulsions containing phospholipids and observe hydrolysis of the fatty acids off of the phospholipids from this heating. Specifically, they describe, at page 775:

> "**Thermal stress was applied by filling heating block chambers** (Dry Baths, Fisher Scientific, Itasca, IL; 60 chambers per block, each 12 mm diameter and 50 mm deep) **with oil and immersing the 2-mL ampoules** containing the emulsion at the desired temperature, covering the blocks with aluminum foil to minimize thermal fluctuation" (emphasis added).

Such a protocol would allow effective heat transfer to the samples because it relies on conduction through hot oil, as was performed in obtaining the data presented in the prosecution of U.S. 8,030,348. Gundersen did not follow this known protocol.

13. In my expert opinion, the ineffective heating applied by Gundersen had a significant effect on the extent of hydrolysis of the ester bonds connecting fatty acids (*e.g.* DHA and EPA) to the glycerol backbone of the phospholipids. Accordingly, Gundersen only allegedly observed a residual mass spectrometry signal of phospholipids bearing DHA and EPA (or EPA/EPA or DHA/DHA).

14. Further, I also note that Gundersen provides an unclear trend as to the effect of heating. Comparing the HPLC-MS data presented in Appendix A, Gundersen appears to detect the same intensity peaks for non-heated, heated to 60°C or 70°C, and heated to 125°C (*see, e.g.*, chromatograms labeled P308-1, P308-2, and P308-3). This further underscores the ineffective heating approach used by Gundersen.

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[4] As noted in ¶4 above, I reviewed the office Action response filed on May 31, 2011 in the prosecution of the U.S. Patent 8,030,348.

[5] Herman and Groves, "The Influence of Free Fatty Acid Formation on the pH of Phospholipid-stabilized Triglyceride Emulsions," *Pharmaceutical Research*, 10(5): 774-76 (1993), **Appendix E.**

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