Attorney Docket No. NEPN-003/00US 313663-2015 (AKBM-32174) **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Patent of:	SAMPALIS, Fotini	Confirmation No.:	1897
Control No.:	95/001,774	Group Art Unit:	3991
Filed:	October 19, 2011	Examiner:	CAMPELL, Bruce R.

FOR: **INTER PARTES REEXAM OF U.S. PATENT 8,030,348: 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 FOTINI SAMPALIS, M.D., PH.D. UNDER 37 C.F.R. § 1.132

I, Fotini Sampalis, declare as follows:

1. I am a Canadian citizen.

2. I studied for my Bachelor's degree in Physiology in McGill University in Montréal, Canada. I have obtained a Doctor of Medicine degree in May of 1988 from the University of Patras in Greece. Following this degree, I undertook my residency in the Pediatric Surgery Department of the Pediatric Surgery Clinic P. and Aglaia Kyriakou Athens Pediatric Hospital in Greece from September, 1992 to July, 1994. I also completed a second residency from July, 1994 to July, 1997 in General Surgery at the University General Pediatric Hospital in Greece. I subsequently obtained a Doctorate in Surgery in September of 1997 from the University of Athens in Greece. Finally, I also obtained a Ph.D. in Experimental Surgery in June of 2006 from McGill University.

3. To date I have obtained numerous special honors, awards, and recognition. I have also had numerous publications and presented many papers, all of which are listed on my Curriculum Vitae, enclosed herewith (**Appendix A**).

4. I am the inventor of numerous patents, including a number in the area of marine extracts. I am the sole inventor of the present patent (U.S. 8,030,348).

5. I am currently the Chief Scientific Officer of Neptune Technologies & Bioressources, Inc. ("Neptune"). Neptune is the sole assignee of the present patent. Further, I am the President of the Neptune subsidiary Acasti Pharma Inc.

6. I have been asked to discuss the experiments that were reported in the '348 patent. Specifically, I have been asked to recount the extraction protocol used in the patent to obtain a krill oil extract.

7. To do so, I briefly recount my initial involvement in Neptune's pursuit of a commercial krill oil. I joined Neptune in the late-1990s/early-2000s, when it was practically the only company with significant commercial interest in krill oil. I was tasked with establishing whether krill oil had medical benefits and made the initial discoveries that it has many.[1] In doing this, I improved the krill oil extraction process, and by deviating from prior processes (including those of Beaudoin), I discovered a krill oil extract that uniquely contained substantial amounts of phospholipids bearing omega-3 fatty acids (such as EPA and DHA) and was suitable for human consumption.

8. I achieved this breakthrough, in part, by avoiding the use of heat during the extraction process. Heat was conventionally used in such processes to remove extraction solvents such as ethanol and acetone, which are not suitable for human consumption in significant amounts. Temperatures of at least 60°C to 70°C were considered necessary for removal of these solvents, and temperatures of 100°C and above were often employed for their removal, as in Beaudoin (*see* WO 00/23456, pages 7 and 10). However, these same temperatures lead to hydrolysis of the key phospholipids. By avoiding substantial hydrolysis of phospholipids,

[1] *See, e.g.,* Sampalis *et al.*, "Evaluation of the Effects of Neptune Krill Oil™ on the Management of Premenstrual Syndrome and Dysmenorrheal" *Altern Med Rev* 8: 171-9 (2003) (**Appendix B**); Bunea *et al.*, "Evaluation of the Effects of Neptune Krill Oil on the Clinical Course of Hyperlipidemia" *Altern Med Rev* 9(4): 420-28 (2004) (**Appendix C**).

I discovered the recited composition and the superior efficacy of extracts containing significant levels of this phospholipid.

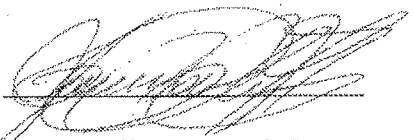
9. The experiments in the '348 patent were conducted under my direction. Our research made me particularly cognizant of the need to remove solvent, to make the extract suitable for human consumption, while avoiding heating, to prevent hydrolysis of the key phospholipids. Accordingly, I directed the extractions of the '348 patent to be conducted at temperatures no higher than 5°C. *See* the '348 Patent, Column 18, Lines 23-67. Particularly, I avoided the use of heat to remove solvents, unlike what was done in Beaudoin. *See* Beaudoin, WO 00/23546 at pages 7 and 10. Also, I ensured that, despite not using heat, sufficient solvent was removed, unlike what was taught by Beaudoin. *See* Beaudoin, WO 00/23546, Table 13 (disclosing "volatile matter and moisture levels" of 10% and 6.8% respectively for fractions I and II). To ensure that we overcame these two limitations in the field, our solvent removal employed methods such as rotary evaporation and was conducted in the cold for extensive periods of time.

10. Therefore, I instructed that the solvent evaporation experiments for the '348 patent be conducted using rotary evaporation at temperatures under 5°C. These involved long periods of time to remove sufficient solvent to render the extract suitable for human consumption. However, as reported in the '348 patent, the resultant extracts contained only small amounts of extraction solvent residue, below the lower tolerated level for chronic consumption. *See* '348 Patent, Table 6 (reporting "Solvent residue[:] <25 ppm").

11. Accordingly, among other major advances, the '348 patent encompasses the removal of extraction solvent at low temperatures and thus, unlike prior teachings of others, retains the structural integrity of the key components of the extract and allows the extract to be suitable for human consumption.

[Remainder of the page left intentionally blank]

12. I further declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true, and further, 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 Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of U.S. Patent 8,030,348.

By: 

Fotini Sampalis, M.D., Ph.D.

Dated: March 16, 2012

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Appendix A

Curriculum Vitae of Dr. Fotini Sampalis

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