IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re *Inter Partes* Reexamination of U.S. Patent No. 8,030,348

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

Issued: 4 October 2011 to Sampalis

DECLARATION BY DR. THOMAS GUNDERSEN IN SUPPORT OF REQUEST FOR INTER PARTES REEXAMINATION OF U.S. PATENT NO. 8,030,348

EFS WEB Filed

Mail Stop Inter Partes Reexam
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Dr. Thomas Gundersen, state as follows:

1. My present position is CEO of Vitas AS - Analytical Pharma Services, Oslo, Norway. My Curriculum Vitae is attached hereto as Exhibit 1.

2. I was asked by Aker Biomarine ASA to analyze lipid fractions extracted from two species of krill, *Euphausia superba* and *Euphausia pacifica*, to determine whether they contain phospholipids that have either eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA) at both the sn-1 and sn-2 positions of the phospholipid molecule. I did not prepare these fractions, but it is my understanding that they were obtained by the procedures described in Beaudoin I (WO 00/23546), Beaudoin II (Canadian Application 2,251,265) and Maruyama (Japanese Laid Open Application 2909508). The results of this analysis are attached hereto as Exhibit 2.

3. As described in Exhibit 2, fractions produced according to either the Beaudoin I or Beaudoin II processes were either left unheated or heated to either 70°C for 5 minutes or 125°C for 15 minutes as described in Beaudoin I and II. The Maruyama fractions were not heated.

4. As described in detail in Exhibit 2, I selected RP-HPLC, HPLC-MS/MS and Multiple Reaction Monitoring (MRM) to analyze the lipid fractions for the presence of phosphatidylcholine (PC) containing EPA at both sn-1 and sn-2 positions (PC-EPA/EPA), phosphatidylcholine with EPA at the sn-1 position and DHA at the sn-2 position or vice versa (PC-EPA/DHA, PC-DHA/EPA), and phosphatidylcholine with DHA at both of the sn-1 and sn-2 positions (PC-DHA/DHA). PC-EPA/EPA and PC-DHA/DHA (99% pure, Sigma Aldrich MO, USA) were used as reference standards. It is important to use reference standards and positive controls to verify that the analytical procedures are working and will perform their intended purpose. It is especially important to optimize mass spectrometric parameters using reference compounds.

PC-EPA/EPA has a predicted molecular weight of 825.6, PC-EPA/DHA has a predicted molecular weight of 851.6, and PC-DHA/DHA has a predicted molecular weight of 877.6. The structures of the substances with molecular mass 825.6, 851.6 and 877.6 were examined by the use of RP- HPLC-MS/MS. An Agilent technologies high end linear tandem mass spectrometer (Agilent 6460 triple Quad) was interfaced with RP-HPLC using ESI ionisation in positive mode. Product ion scans of the protonated parent molecular weights (826.6 and 878.6) were then taken up for the reference standards. These data were then used as a basis for selection of multiple reaction monitoring (MRM) transitions and reconstructed ion chromatograms from the transitions described in the following were taken up. The transitions were chosen to allow us to determine whether the lipid is a phospahtidylcholine species and whether both the Sn-1 and Sn-2 positions on the phospholipid are occupied by either EPA or DHA.

R-ID	PL-Species	Retention time*	Parent mass [M+1]	Loss off	MRM ID	MRM
218	PC-EPA/EPA	3.61	827.6	EPA	1	827.6/524
n.a.	PC-EPA/DHA	*	852.6	EPA	2	852.6/550
n.a.	PC-EPA/DHA	*	852.6	DHA	3	852.6/524
219	PC-DHA/DHA	3.94	878.6	DHA	4	878.6/550

*HPLC-MS/MS system

5. Use of single quadrupole MS showed that all samples (with the exception of the ethyl acetate extracts from *E. pacifica*) contained lipids that matched either the theoretical molecular weight (PC-EPA/DHA) or both molecular and theoretical weight and the chromatographic retention time of

reference standards (PC-EPA/EPA, PC-DHA/DHA). The *E. pacifica* ethyl acetate fractions contained very little material. It is not unlikely that something has not worked according to the procedure during the extraction of the *E. pacifica* krill samples and it is doubtful that these samples were representative samples. This assumption is supported by the fact that ethanol extraction of the same sample type gave a much higher yield and that ethyl acetate extraction of the same type of sample but with E.Superba instead of *E. pacifica* also gave a high yield. The extraction should have been repeated but there was not enough time for this. However, it is expected that if sufficient amount of material had been used for the analysis the three phospholipid species would have been present as they were in the *E. pacifica* ethanol fractions and in the E.Superba ethyl acetate fractions.

All samples were analyzed with MRM on the triple quadrupole, the criteria for positive identification was a positive signal at the correct retention time for the different MRMs as shown in the Table below (e.g., for PC-EPA/EPA a positive signal was required for [825+1]→184 and MRM1). Full results for all samples are shown in the following Table.

Vitas ID	**Frac. #**	**Treatment °C/min**	**MRMs** [825+H]→184 [851+H]→184 [877+H]→184	**MRM 1** PC-EPA/EPA 826→524	**MRM 2** PC-EPA/DHA 852→524	**MRM 3** PC-EPA/DHA 852→550	**MRM 4** PC-DHA/DHA 878→550	**Conclusion**
P308-1	**IIa**	none	YES YES YES	YES	YES	YES	YES	Contains PC-EPA/EPA Contains PC-EPA/DHA Contains PC-DHA/DHA
P308-2	**IIa**	70/5	YES YES YES	YES	YES	YES	YES	Contains PC-EPA/EPA Contains PC-EPA/DHA Contains PC-DHA/DHA
P308-3	**IIa**	125/15	YES YES YES	YES	YES	YES	YES	Contains PC-EPA/EPA Contains PC-EPA/DHA Contains PC-DHA/DHA
P308-4	**IIb**	none	NO NO NO	NO	NO	NO	NO	n.d. PC-EPA/EPA n.d. PC-EPA/DHA n.d. PC-DHA/DHA
P308-5	**IIb**	70/5	NO NO NO	NO	NO	NO	NO	n.d. PC-EPA/EPA n.d. PC-EPA/DHA n.d. PC-DHA/DHA

P308-6	**IIb**	125/15	NO NO NO	NO	NO	NO	NO	n.d. PC-EPA/EPA n.d. PC-EPA/DHA n.d. PC-DHA/DHA
P308-7	**IIa**	none	YES YES YES	YES	YES	YES	YES	Contains PC-EPA/EPA Contains PC-EPA/DHA Contains PC-DHA/DHA
P208-8	**IIa**	70/5	YES YES YES	YES	YES	YES	YES	Contains PC-EPA/EPA Contains PC-EPA/DHA Contains PC-DHA/DHA
P308-9	**IIa**	125/15	YES YES YES	YES	YES	YES	YES	Contains PC-EPA/EPA Contains PC-EPA/DHA Contains PC-DHA/DHA
P308-10	**IIb**	none	YES YES YES	YES	YES	YES	YES	Contains PC-EPA/EPA Contains PC-EPA/DHA Contains PC-DHA/DHA
P308-11	**IIb**	70/5	YES YES YES	YES	YES	YES	YES	Contains PC-EPA/EPA Contains PC-EPA/DHA Contains PC-DHA/DHA
P308-12	**IIb**	125/15	YES YES YES	YES	YES	YES	YES	Contains PC-EPA/EPA Contains PC-EPA/DHA Contains PC-DHA/DHA
P308-13	**n.a.**	n.a.	YES YES YES	YES	YES	YES	YES	Contains PC-EPA/EPA Contains PC-EPA/DHA Contains PC-DHA/DHA
P308-14	**n.a.**	n.a.	YES YES YES	YES	YES	YES	YES	Contains PC-EPA/EPA Contains PC-EPA/DHA Contains PC-DHA/DHA
P308-15	**n.a.**	n.a.	YES YES YES	YES	YES	YES	YES	Contains PC-EPA/EPA Contains PC-EPA/DHA Contains PC-DHA/DHA
P308-16	**n.a.**	n.a.	YES YES YES	YES	YES	YES	YES	Contains PC-EPA/EPA Contains PC-EPA/DHA Contains PC-DHA/DHA

6. In summary, these results demonstrate that each of the lipid fractions tested (with the exception of the ethyl acetate extracts from *E. pacifica*) contain the following phospholipid species: PC-EPA/EPA; PC-EPA/DHA; and PC-DHA/DHA.

7. I further declare that all statement 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 the application or any patent issued thereon.

Respectfully submitted,

Thomas S Gundersen

Dr. Thomas Gundersen

Date: October 4, 2011

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.