

## **APPENDIX A**

# MATERIAL SAFETY DATA SHEET

## SECTION I - PRODUCT IDENTIFICATION

**Product Name:** Marine Oil

**Product Use:** Dietary supplement

**WHMIS Class:** Not Controlled

**TDG Classification:** Not Regulated

<b>Manufacturer/Supplier:</b>	Neptune Technologies & Bioresources
<b>Address:</b>	500 boul Saint-Martin Ouest Bureau 550
<b>Telephone:</b>	450 - 972-6291519

## SECTION II - HAZARDOUS INGREDIENTS

Ingredients	CAS#	Wt%	OSHA-PEL	ACGIH-TLV	LC 50	LD 50
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None by WHMIS/OSHA criteria.

## SECTION III - PHYSICAL DATA

<b>Boiling Point (°C):</b> Not available	<b>Specific Gravity (20 = 1):</b> Not available
<b>Vapour Pressure (mm Hg):</b> Not available	<b>% Volatile (Wt %):</b> Not available
<b>Vapour Density (Air = 1):</b> Not available	<b>Evaporation Rate (Ether = 1):</b> Not available
<b>Solubility in Water:</b> Insoluble	<b>pH (100%):</b> Not available
<b>Physical State:</b> Liquid	<b>Viscosity:</b> Viscous
<b>Appearance:</b> Brown	<b>Odour Threshold (ppm):</b> Not available

## SECTION IV - FIRE AND EXPLOSION DATA

**Flammability:** Not flammable by WHMIS/OSHA criteria.  
**Flash Point (°C, TCC):** None    **LEL:** Not applicable    **UEL:** Not applicable  
**Hazardous Combustion Products:** May include and are not limited to oxides of carbon  
**Autoignition Temperature (°C):** Not applicable  
**Means of Extinction:** Treat for surrounding material.  
**Special Fire Hazards:** Firefighters should wear self-contained breathing apparatus.

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**SECTION V - REACTIVITY DATA**

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**Conditions for Chemical Instability:** Stable.  
**Incompatible Materials:** None known.  
**Reactivity, and Under What Conditions:** Not available.  
**Hazardous Decomposition Products:** May include and are not limited to oxides of carbon when heated to  
Decomposition

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**SECTION VI - TOXICOLOGICAL PROPERTIES**

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**Route of Entry:** Eye, Skin contact, Inhalation, Ingestion.

**EFFECTS OF ACUTE EXPOSURE:**

**Eye:** May cause irritation upon direct contact.  
**Skin:** May cause irritation upon direct contact.  
**Inhalation:** May cause respiratory tract irritation.  
**Ingestion:** May cause stomach distress, nausea or vomiting if ingested in large quantities.

**EFFECTS OF CHRONIC EXPOSURE:**

**Skin:** Prolonged or repeated exposure can cause drying, defatting and dermatitis.  
**Irritancy:** Non-hazardous by WHMIS/OSHA criteria.  
**Respiratory Tract Sensitization:** No data available.  
**Carcinogenicity:** Non-hazardous by WHMIS/OSHA criteria.  
**Teratogenicity, Mutagenicity, Reproductive Effects:** No data available.  
**Synergistic Materials:** Not available.

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**SECTION VII- PREVENTATIVE MEASURES**

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**Gloves:** No requirements beyond standard industrial hygiene practices.  
**Eye Protection:** No requirements beyond standard industrial hygiene practices.  
**Respiratory Protection:** Not normally required if good ventilation is maintained.  
**Other Protective Equipment:** As required by employer code.  
**Engineering Controls:** General ventilation normally adequate.  
**Leak and Spill Procedure:** Before attempting clean up, refer to hazard data given above. Small spills may be absorbed with non-reactive absorbent and placed in suitable, covered, labelled containers. Prevent large spills from entering sewers or waterways. Contact emergency services and supplier for advice.  
**Waste Disposal:** Review federal, state/provincial, and local government requirements prior to disposal.  
**Storage and Handling Requirements:** Keep out of reach of children. Store in a closed container away from incompatible materials.

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**SECTION VIII - FIRST AID**

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**Eye:** Flush with cool water. Remove contact lenses, if applicable, and continue flushing. Obtain medical attention if irritation

persists.

**Skin:** Flush with cool water. Wash with soap and water. Obtain medical attention if irritation persists.

**Inhalation:** If symptoms develop move victim to fresh air. If symptoms persist, obtain medical attention.

**Ingestion:** Do not induce vomiting. Rinse mouth with water then drink one or two glasses of water. Obtain medical attention.

Never give anything by mouth if victim is unconscious, or is convulsing.

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**SECTION IX - PREPARATION INFORMATION**

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Date: 2002/01/24

MSDS Prepared by: KGK SYNERGIZE INC.

Telephone: 1 - 519- 438-9374

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**Disclaimer**

Information for this material safety data sheet was obtained from sources considered technically accurate and reliable. While every effort has been made to ensure full disclosure of product hazards, in some cases data is not available and is so stated. Since conditions of actual product use are beyond control of the supplier, it is assumed that users of this material have been fully trained according to the mandatory requirements of WHMIS. No warranty, expressed or implied, is made and supplier will not be liable for any losses, injuries or consequential damages which may result from the use of or reliance on any information contained in this form. If user requires independent information on ingredients in this or any other material, we recommend contact with the Canadian Centre for Occupational Health and Safety (CCOHS) in Hamilton, Ontario (1-905-572-4400) or CSST in Montreal, Quebec (514-873-3990).

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# MATERIAL SAFETY DATA SHEET

## SECTION I - PRODUCT IDENTIFICATION

**Product Name:** Krill Protein

**Product Use:** Dietary supplement

**WHMIS Class:** Not Controlled

**TDG Classification:** Not Regulated

**Manufacturer/Supplier:** Neptune Technologies & Bioresources  
**Address:** 500 boul Saint-Martin Ouest  
 Bureau 550  
 Laval, Quebec, H7M 3Y2  
**Telephone:** 450 - 972-6291

## SECTION II - HAZARDOUS INGREDIENTS

<u>Ingredients</u>	<u>CAS#</u>	<u>Wt%</u>	<u>OSHA-PEL</u>	<u>ACGIH-TLV</u>	<u>LC 50</u>	<u>LD 50</u>
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None by WHMIS/OSHA criteria.

## SECTION III - PHYSICAL DATA

<b>Boiling Point (°C):</b> Not applicable	<b>Specific Gravity (H2O = 1):</b> Not available
<b>Vapour Pressure (mm Hg):</b> Not applicable	<b>% Volatile (Wt %):</b> Not available
<b>Vapour Density (Air = 1):</b> Not applicable	<b>Evaporation Rate (Ether = 1):</b> Not applicable
<b>Solubility in Water:</b> Not available	<b>pH (100%):</b> Not available
<b>Physical State:</b> Solid	<b>Viscosity:</b> Not applicable
<b>Appearance:</b> Off-white powder	<b>Odour Threshold (ppm):</b> Not available

## SECTION IV - FIRE AND EXPLOSION DATA

**Flammability:** Not flammable by WHMIS/OSHA criteria.  
**Flash Point (°C, TCC):** None    **LEL:** Not applicable    **UEL:** Not applicable  
**Hazardous Combustion Products:** May include and are not limited to oxides of carbon.  
**Autoignition Temperature (°C):** Not applicable  
**Means of Extinction:** Treat for surrounding material.  
**Special Fire Hazards:** Firefighters should wear self-contained breathing apparatus.

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**SECTION V - REACTIVITY DATA**

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**Conditions for Chemical Instability:** Stable.

**Incompatible Materials:** None known.

**Reactivity, and Under What Conditions:** Not available.

**Hazardous Decomposition Products:** May include and are not limited to oxides of carbon when heated to decomposition.

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**SECTION VI - TOXICOLOGICAL PROPERTIES**

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**Route of Entry:** Eye, Skin contact, Inhalation, Ingestion.

**EFFECTS OF ACUTE EXPOSURE:**

**Eye:** May cause irritation upon direct contact.

**Inhalation:** May cause respiratory tract irritation.

**Ingestion:** May cause stomach distress, nausea or vomiting if ingested in large quantities.

**EFFECTS OF CHRONIC EXPOSURE:**

**Skin:** Prolonged or repeated exposure can cause drying, defatting and dermatitis.

**Irritancy:** Non-hazardous by WHMIS/OSHA criteria.

**Respiratory Tract Sensitization:** No data available.

**Carcinogenicity:** Non-hazardous by WHMIS/OSHA criteria.

**Teratogenicity, Mutagenicity, Reproductive Effects:** No data available.

**Synergistic Materials:** Not available.

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**SECTION VII- PREVENTATIVE MEASURES**

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**Gloves:** No requirements beyond standard industrial hygiene practices.

**Eye Protection:** No requirements beyond standard industrial hygiene practices.

**Respiratory Protection:** Not normally required if good ventilation is maintained.

**Other Protective Equipment:** As required by employer code.

**Engineering Controls:** General ventilation normally adequate.

**Leak and Spill Procedure:** Before attempting clean up, refer to hazard data given above. Use broom or dry vacuum to

collect material for proper disposal without raising dust. Rinse area with water. Prevent large spills from entering sewers or

waterways. Contact emergency services and supplier for advice.

**Waste Disposal:** Review federal, state/provincial, and local government requirements prior to disposal.

**Storage and Handling Requirements:** Keep out of reach of children. Store in a closed container away from incompatible materials.

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**SECTION VIII - FIRST AID**

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**Eye:** Flush with cool water. Remove contact lenses, if applicable, and continue flushing. Obtain medical attention if irritation persists.

**Skin:** Brush away excess of dry material. Flush with water. Obtain medical attention if irritation persists.

**Inhalation:** If symptoms develop move victim to fresh air. If symptoms persist, obtain medical attention.

**Ingestion:** Do not induce vomiting. Rinse mouth with water then drink one or two glasses of water. Obtain medical attention.

Never give anything by mouth if victim is unconscious, or is convulsing.

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**SECTION IX - PREPARATION INFORMATION**

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**Date:** 2002/01/24

**MSDS Prepared by:** KGK SYNERGIZE INC.

**Telephone:** 1 - 519 -438-9374

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# MATERIAL SAFETY DATA SHEET

## SECTION I - PRODUCT IDENTIFICATION

**Product Name:** Freeze Dried Krill

**Product Use:** Dietary supplement

**WHMIS Class:** Not Controlled

**TDG Classification:** Not Regulated

**Manufacturer/Supplier:** Neptune Technologies & Bioresources  
**Address:** 500 boul Saint-Martin Ouest  
Bureau 550  
Laval, Quebec, H7M 3Y2  
**Telephone:** 450 - 972-6291

## SECTION II - HAZARDOUS INGREDIENTS

<u>Ingredients</u>	<u>CAS#</u>	<u>Wt%</u>	<u>OSHA-PEL</u>	<u>ACGIH-TLV</u>	<u>LC 50</u>	<u>LD 50</u>
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None by WHMIS/OSHA criteria.

## SECTION III - PHYSICAL DATA

<b>Boiling Point (°C):</b> Not applicable	<b>Specific Gravity (H<sub>2</sub>O = 1):</b> Not available
<b>Vapour Pressure (mm Hg):</b> Not applicable	<b>% Volatile (Wt %):</b> Not available
<b>Vapour Density (Air = 1):</b> Not applicable	<b>Evaporation Rate (Ether = 1):</b> Not applicable
<b>Solubility in Water:</b> Not available	<b>pH (100%):</b> Not available
<b>Physical State:</b> Solid	<b>Viscosity:</b> Not applicable
<b>Appearance:</b> Off-white powder	<b>Odour Threshold (ppm):</b> Not available

## SECTION IV - FIRE AND EXPLOSION DATA

**Flammability:** Not flammable by WHMIS/OSHA criteria.  
**Flash Point (°C, TCC):** None    **LEL:** Not applicable    **UEL:** Not applicable  
**Hazardous Combustion Products:** May include and are not limited to oxides of carbon.  
**Autoignition Temperature (°C):** Not applicable  
**Means of Extinction:** Treat for surrounding material.  
**Special Fire Hazards:** Firefighters should wear self-contained breathing apparatus.

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**SECTION V - REACTIVITY DATA**

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**Conditions for Chemical Instability:** Stable.  
**Incompatible Materials:** None known.  
**Reactivity, and Under What Conditions:** Not available.  
**Hazardous Decomposition Products:** May include and are not limited to oxides of carbon when heated to decomposition.

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**SECTION VI - TOXICOLOGICAL PROPERTIES**

=====

**Route of Entry:** Eye, Skin contact, Inhalation, Ingestion.

**EFFECTS OF ACUTE EXPOSURE:**

**Eye:** May cause irritation upon direct contact.  
**Inhalation:** May cause respiratory tract irritation.  
**Ingestion:** May cause stomach distress, nausea or vomiting if ingested in large quantities.

**EFFECTS OF CHRONIC EXPOSURE:**

**Skin:** Prolonged or repeated exposure can cause drying, defatting and dermatitis.  
**Irritancy:** Non-hazardous by WHMIS/OSHA criteria.  
**Respiratory Tract Sensitization:** No data available.  
**Carcinogenicity:** Non-hazardous by WHMIS/OSHA criteria.  
**Teratogenicity, Mutagenicity, Reproductive Effects:** No data available.  
**Synergistic Materials:** Not available.

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**SECTION VII- PREVENTATIVE MEASURES**

=====

**Gloves:** No requirements beyond standard industrial hygiene practices.  
**Eye Protection:** No requirements beyond standard industrial hygiene practices.  
**Respiratory Protection:** Not normally required if good ventilation is maintained.  
**Other Protective Equipment:** As required by employer code.  
**Engineering Controls:** General ventilation normally adequate.  
**Leak and Spill Procedure:** Before attempting clean up, refer to hazard data given above. Use broom or dry vacuum to collect material for proper disposal without raising dust. Rinse area with water. Prevent large spills from entering sewers or waterways. Contact emergency services and supplier for advice.  
**Waste Disposal:** Review federal, state/provincial, and local government requirements prior to disposal.  
**Storage and Handling Requirements:** Keep out of reach of children. Store in a closed container away from incompatible materials.

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**SECTION VIII - FIRST AID**

=====

**Eye:** Flush with cool water. Remove contact lenses, if applicable, and continue flushing. Obtain medical attention if irritation persists.

**Skin:** Brush away excess of dry material. Flush with water. Obtain medical attention if irritation persists.

**Inhalation:** If symptoms develop move victim to fresh air. If symptoms persist, obtain medical attention.

**Ingestion:** Do not induce vomiting. Rinse mouth with water then drink one or two glasses of water. Obtain medical attention.

Never give anything by mouth if victim is unconscious, or is convulsing.

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**SECTION IX - PREPARATION INFORMATION**

=====

**Date:** 2002/01/24

**MSDS Prepared by:** KGK SYNERGIZE INC.

**Telephone:** 1 - 519 -438-9374

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[Code of Federal Regulations]  
[Title 21, Volume 1, Parts 1 to 99]  
[Revised as of April 1, 2000]  
From the U.S. Government Printing Office via GPO Access  
[CITE: 21CFR73.75]

[Page 337-338]

TITLE 21--FOOD AND DRUGS

PART 73--LISTING OF COLOR ADDITIVES EXEMPT FROM CERTIFICATION--Table of Contents

Subpart A--Foods

Sec. 73.75 Canthaxanthin.

(a) Identity. (1) The color additive canthaxanthin is <greek-b>-carotene-4,4'-dione.

(2) Color additive mixtures for food use made with canthaxanthin may contain only those diluents that are suitable and that are listed in this subpart as safe for use in color additive mixtures for coloring foods.

(b) Specifications. Canthaxanthin shall conform to the following specifications and shall be free from impurities other than those named to the extent that such other impurities may be avoided by good manufacturing practice:

Physical state, solid.

1 percent solution in chloroform, complete and clear.

Melting range (decomposition), 207 deg.C. to 212 deg.C. (corrected).

Loss on drying, not more than 0.2 percent.

Residue on ignition, not more than 0.2 percent.

Total carotenoids other than trans-canthaxanthin, not more than 5 percent.

Lead, not more than 10 parts per million.

Arsenic, not more than 3 parts per million.

Mercury, not more than 1 part per million.

Assay, 96 to 101 percent.

(c) Use and restrictions. (1) The color additive canthaxanthin may be safely

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used for coloring foods generally subject to the following restrictions:

(i) The quantity of canthaxanthin does not exceed 30 milligrams per pound of solid or semisolid food or per pint of liquid food; and

(ii) It may not be used to color foods for which standards of identity have been promulgated under section 401 of the act unless added color is authorized by such standards.

(2) Canthaxanthin may be safely used in broiler chicken feed to enhance the yellow color of broiler chicken skin in accordance with the

following conditions: The quantity of canthaxanthin incorporated in the feed shall not exceed 4.41 milligrams per kilogram (4 grams per ton) of complete feed to supplement other known sources of xanthophyll and associated carotenoids to accomplish the intended effect.

(3) Canthaxanthin may be safely used in the feed of salmonid fish in accordance with the following prescribed conditions:

(i) Canthaxanthin may be added to the fish feed only in the form of a stabilized color additive mixture;

(ii) The color additive is used to enhance the pink to orange-red color of the flesh of salmonid fish; and

(iii) The quantity of color additive in feed shall not exceed 80 milligrams per kilogram (72 grams per ton) of finished feed.

(d) Labeling requirements. (1) The labeling of the color additive and any mixture prepared therefrom intended solely or in part for coloring purposes shall conform to the requirements of Sec. 70.25 of this chapter.

(2) For purposes of coloring fish, the labeling of the color additive and any premixes prepared therefrom shall bear expiration dates (established through generally accepted stability testing methods) for the sealed and open container, other information required by Sec. 70.25 of this chapter, and adequate directions to prepare a final product complying with the limitations prescribed in paragraph (c)(3) of this section.

(3) The presence of the color additive in finished fish feed prepared according to paragraph (c)(3) of this section shall be declared in accordance with Sec. 501.4 of this chapter.

(4) The presence of the color additive in salmonid fish that have been fed feeds containing canthaxanthin shall be declared in accordance with Secs. 101.22(b), (c), and (k)(2), and 101.100(a)(2) of this chapter.

(e) Exemption from certification. Certification of this color additive is not necessary for the protection of the public health, and therefore batches thereof are exempt from the certification requirements of section 721(c) of the act.

[42 FR 15643, Mar. 22, 1977, as amended at 50 FR 47534, Nov. 19, 1985; 63 FR 14817, Mar. 27, 1998]

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## Color Additive Regulations

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[Title 21, Volume 1, Parts 1 to 99]  
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[CITE: 21CFR73.1075]

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## TITLE 21--FOOD AND DRUGS

### PART 73--LISTING OF COLOR ADDITIVES EXEMPT FROM CERTIFICATION--Table of Contents

#### Subpart B--Drugs

#### Sec. 73.1075 Canthaxanthin.

(a) Identity and specifications. (1) The color additive canthaxanthin shall conform in identity and specifications to the requirements of Sec. 73.75(a)(1) and (b).

(2) Color additive mixtures for ingested drug use made with canthaxanthin may contain only those diluents that are suitable and that are listed in this subpart as safe in color additive mixtures for coloring ingested drugs.

(b) Uses and restrictions. Canthaxanthin may be safely used for coloring ingested drugs generally in amounts consistent with good manufacturing practice.

(c) Labeling requirements. The label of the color additive and of any mixtures prepared therefrom intended solely or in part for coloring purposes shall conform to the requirements of Sec. 70.25 of this chapter.

(d) Exemption from certification. Certification of this color additive is not necessary for the protection of the public health, and therefore batches thereof are exempt from the certification requirements of section 721(c) of the act.

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[Code of Federal Regulations]  
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[CITE: 21CFR73.35]

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TITLE 21--FOOD AND DRUGS

PART 73--LISTING OF COLOR ADDITIVES EXEMPT FROM CERTIFICATION--Table of Contents

Subpart A--Foods

Sec. 73.35 Astaxanthin.

(a) Identity. (1) The color additive astaxanthin is 3, 3'-dihydroxy-<greek-b>, <greek-b>-carotene-4, 4'-dione.

(2) Astaxanthin may be added to the fish feed only as a component of a stabilized color additive mixture. Color additive mixtures for fish feed use made with astaxanthin may contain only those diluents that are suitable and are listed in this subpart as safe for use in color additive mixtures for coloring foods.

(b) Specifications. Astaxanthin shall conform to the following specifications and shall be free from impurities other than those named to the extent that such impurities may be avoided by good manufacturing practice:

Physical state, solid.

0.05 percent solution in chloroform, complete and clear.

Absorption maximum wavelength 484-493 nanometers (in chloroform).

Residue on ignition, not more than 0.1 percent.

Total carotenoids other than astaxanthin, not more than 4 percent.

Lead, not more than 5 parts per million.

Arsenic, not more than 2 parts per million.

Mercury, not more than 1 part per million.

Heavy metals, not more than 10 parts per million.

Assay, minimum 96 percent.

(c) Uses and restrictions. Astaxanthin may be safely used in the feed of salmonid fish in accordance with the following prescribed conditions:

(1) The color additive is used to enhance the pink to orange-red color of the flesh of salmonid fish.

(2) The quantity of color additive in feed is such that the color additive shall not exceed 80 milligrams per kilogram (72 grams per ton) of finished feed.

(d) Labeling requirements. (1) The labeling of the color additive and any premixes prepared therefrom shall bear expiration dates for the sealed and open container (established through generally accepted stability testing methods), other information required by Sec. 70.25 of this chapter, and adequate directions to prepare a final product

complying with the limitations prescribed in paragraph (c) of this section.

(2) The presence of the color additive in finished fish feed prepared according to paragraph (c) of this section shall be declared in accordance with Sec. 501.4 of this chapter.

(3) The presence of the color additive in salmonid fish that have been fed feeds containing astaxanthin shall be declared in accordance with Secs. 101.22(k)(2) and 101.100(a)(2) of this chapter.

(e) Exemption from certification. Certification of this color additive is not necessary for the protection of the public health, and therefore batches thereof are exempt from the certification requirements of section 721(c) of the act.

[60 FR 18738, Apr. 13, 1995]

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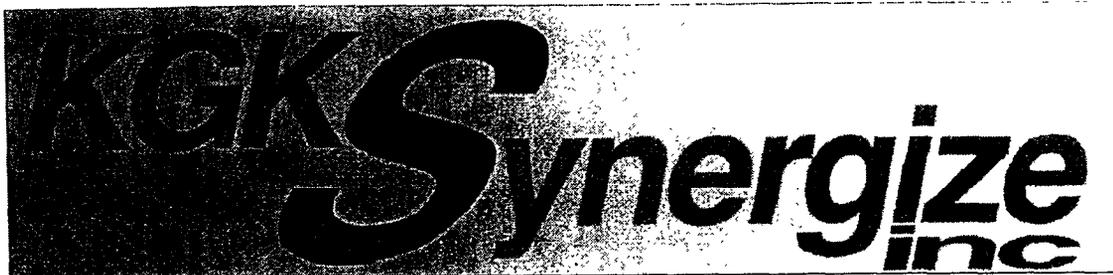
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## Color Additive Regulations

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## ANALYTICAL REPORT

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Client	Louis Lappointte
Company	Neptune Technologies & Bioressources Inc.
Date Received	November 14, 2001.
Date Reported	November 22, 2001.

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Analysis of astaxanthin and canthaxanthin was performed on the following samples submitted with your order

Sample name	Type of sample
800	Marine oil
801	Marine oil

The following reference method was used

Enzymatic hydrolysis using Lipase from *Candida rugosa* followed by extraction and high performance liquid chromatography.

#### References

Xinia et al. J, Food Comp. Anal. 13 (2000), 179-187.

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	800	801
Canthaxanthin $\mu\text{g/g}$	389.3	454.2
Astaxanthin $\mu\text{g/g}$	168.7	122.3

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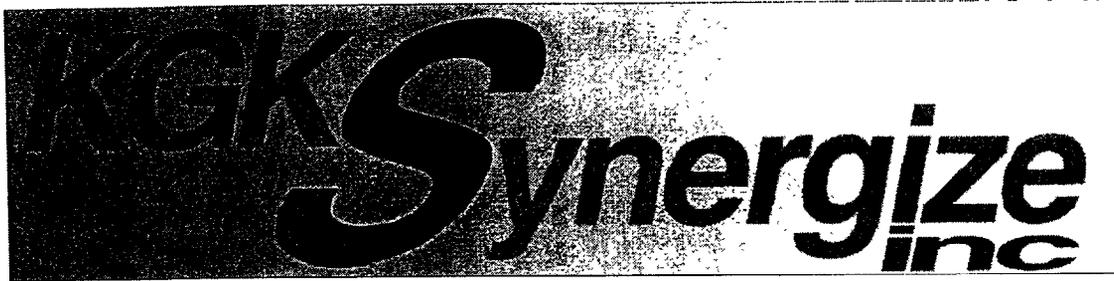
This report has been approved by:

A handwritten signature in black ink, appearing to read 'Elzbieta M. Kurowska'.

Elzbieta M. Kurowska, Ph.D.  
Vice President, Research & Development

Suite 1030, One London Place, 255 Queens Avenue, London, ON N6A 5R8 Canada Tel: (519) 438-9374  
or (519) 438-8916 Fax: (519) 438-8314 E-mail: [kurowska@kgksynergize.com](mailto:kurowska@kgksynergize.com) [www.kgksynergize.com](http://www.kgksynergize.com)





## ANALYTICAL REPORT

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Client	Louis Lappointte
Company	Neptune Technologies & Bioressources Inc.
Date Received	November 14, 2001.
Date Reported	November 23, 2001.

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Trace metal analysis was performed on the following samples submitted with your order

Sample name	Type of sample
800	Marine oil
801	Marine oil

The following reference method has been used

Digestion by nitric acid and hydrogen peroxide followed by ICP-MS (Inductively Coupled Plasma Mass Spectrometry)

This report has been approved by:

A handwritten signature in black ink, appearing to read 'Elzbieta M. Kurowska'.

Elzbieta M. Kurowska, Ph.D.  
Vice President, Research & Development

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	800	801
<b>Lead <math>\mu\text{g/g}</math></b>	0.005	0.002
<b>Sodium <math>\text{mg/g}</math></b>	0.0023	0.019
<b>Magnesium <math>\mu\text{g/g}</math></b>	0.06	0.03
<b>Iron <math>\mu\text{g/g}</math></b>	0.87	0.41
<b>Copper <math>\mu\text{g/g}</math></b>	0.05	0.09
<b>Zinc <math>\mu\text{g/g}</math></b>	0.06	0.04
<b>Selenium <math>\mu\text{g/g}</math></b>	0.05	0.02
<b>Potassium <math>\text{mg/g}</math></b>	0.015	0.024

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**BIOPHARM inc.**

3885, boul. Industriel, Laval Québec

Canada H7L 4S3

Tél. (450) 663-6724

Télec. (450) 975-8111

# Certificate of analysis

NCA : N18-020408-37

Req : -

Code Client : N18

Version : 1

*Our quality system is certified according to ISO-9002 standard*

Printed : 2002/04/29

Received : 2002/04/08

Date : 2002/04/29

(yyyy/mm/dd)

Page : 1 of 2

**Neptune Technologies/Tina Sampalis**

500, boul. St-Martin Ouest

Laval, Québec H7M 3Y2



## RESULT

**Sample :** MARINE OIL

**Section :** 1

**Lot Not :** WA1303

**Gabarit :** Raw material

**Description :** Reddish opaque oily liquid having a fishy odor

Complies

TEST	METHOD	SPECIFICATION	
Cholesterol	JAOAC Vol. 76, No. 4 (GLC)	Report (g/100 g)	1.3
Vitamin A	HPLC	Report (UI/g)	809.2
Vitamin E	HPLC	Report (UI/g)	1.01
Free fatty acid profile	AOCS Ce 1b-89 (GLC)	Report (%)	(2)
A. .e	GLC	Report (ppm)	< 100
Free fatty acids	USP <401> (1)	Report (mg KOH/g)	29.7
Phosphatidyl inositol	(TLC)	Report (g/100 g)	< 2.5
Phosphatidyl choline	(TLC)	Report (g/100 g)	5.0
Phosphatidyl ethanolamine	(TLC)	Report (g/100 g)	48.5
Phosphatidyl serine	(TLC)	Report (g/100 g)	< 2.5
Sphingomyelin	(TLC)	Report (g/100 g)	< 2.4
Total phospholipids	Colorimetry	Report (g/100 g)	53.5
Iodine value	A.O.C.S. Cd. 1-25	Report (mg I/100g)	3.56
Oil stability index	A.O.C.S. Cd. 12b. 92	Induction time converted to the reference temperature of 97.8°C (hrs)	> 50
p-Anidisine value	A.O.C.S. Cd. 18 90	Report	1.98
Peroxide value	A.O.C.S. Cd. 8b. 90	Report (meq peroxide/kg)	< 0.1
Saponification index	A.O.C.S. Cd 3.25	Report (mg KOH/g)	172.1
Moisture and volatile matter	Dried 16 h at 60°C under vacuum	Report (%)	0.61

(1) Under Acid Value; (2) (100 - % ash), USP Current Edition

Verified by : **Sylvain Mandeville, Ph.D., Scientific Director**

Approved by : **Luce Blanchard, Chemist**

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**BIOPHARM inc.**

3885, boul. Industriel, Laval Québec

Canada H7L 4S3

Tél. (450) 663-6724

Télé. (450) 975-8111

# Certificate of analysis

NCA : N18-020408-37

Req : -

Code Client : N18

Version : 1

*Our quality system is certified according to ISO-9002 standard*

Printed : 2002/04/29

Received : 2002/04/08

Date : 2002/04/29

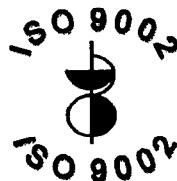
(yyyy/mm/dd)

Page : 2 of 2

**Neptune Technologies/Tina Sampalis**

500, boul. St-Martin Ouest

Laval, Québec H7M 3Y2



## RESULT

**Sample :** MARINE OIL

Viscosity	FP-78	Report (cst)	927.2
Ash (total inorganic substances)	KGK (2h at 600°C)	Report (%)	4.09
Total protein	CA-126-050	Report (%)	6.08
Total lipids	CG-118-039	Report (%)	79.3
Assay of Sodium (AAS)	CM-109-125	Report (mg/100 g)	386
Assay of Zinc (AAS)	CM-109-125	Report (mg/100 g)	0.66
Assay of Potassium (AAS)	CM-109-125	Report (mg/100 g)	207
Assay of Calcium (AAS)	CM-109-125	Report (mg/100 g)	0.60
Assay of Selenium (AAS)	CM-109-215	Report (mg/100 g)	< 3.1
Assay of Aluminium (AA)	CM-109-125	Report (mg/100 g)	7.45
Assay of Copper (AA)	CM-109-125	Report (mg/100 g)	0.17
Assay of Manganese (AAS)	CM-109-125	Report (mg/100 g)	< 0.31

(1) Under Acid Value; (2) (100 - % ash); USP Current Edition

Verified by : **Sylvain Mandeville, Ph.D., Scientific Director**

Approved by : **Lucie Blanchard, Chemist**

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CERTIFICATE OF ANALYSIS



NCA: N18-020408-37  
 Req: -  
 Code client: N18  
 Version: 1

Neptune Technologies  
 500, boul. St-Martin Ouest  
 Laval, Québec H7M 3Y2



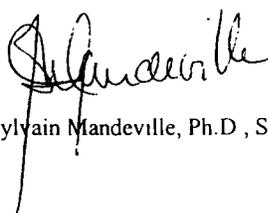
Reçu: 2002/04/08  
 Date: 2002/04/29  
 Section: 2

Échantillon: Marine Oil, lot WA1303

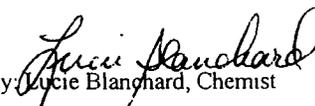
FATTY ACIDS	AREA %	g/100 g of sample
C 14 :0	6.10	4.84
C 14 :1	0.15	0.12
C 15 :0	0.34	0.27
C 16 :0	19.55	15.50
C 16 :1	5.89	4.67
C 18 :0	0.82	0.65
C 18 :1	12.77	10.13
C 18 :2n-6	1.47	1.17
C 18 :4n-6	0.05	0.04
C 18 :3n-3	0.72	0.57
C 18 :4n-3	1.11	0.88
C 20 :0	0.08	0.06
C 20 :1	0.38	0.30
C 20 :2n-6	0.13	0.10
C 20 :4n-6	0.65	0.52
C 20 :4n-3	0.47	0.37

WARNEX | BIOPHARM | NORSCIENCE | GENEVISION |

C 20 :5n-3 (EPA)	23.06	18.30
C 22 :0	0.25	0.20
C 21 :5n-3	7.12	5.64
C 23 :0	1.21	0.96
C 22 :5n-3	0.12	0.09
C 24 :0	1.09	0.87
C 22 :6n-3	12.09	9.58
C 24 :1	0.32	0.25



Verified by: Sylvain Mandeville, Ph.D , Scientific Director



Approved by: Lucie Blanchard, Chemist





185 boul Brunswick  
Pointe-Claire, Québec  
Canada H9R 4Z1  
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## TEST REPORT

NEPTUNE TECHNOLOGIES & BIORESSOURCES INC.  
500, St-Martin ouest, bureau 550  
Laval, Québec  
H7M 3Y2

RECEPTION DATE : 01 11 16  
LABORATORY NUMBER : 160080544R  
NUMBER OF SAMPLES : 5  
REPORT DATE : 01 12 05  
PAGE : 1 DE 1  
ANALYSIS REPORT : 01 11 30

ATTENTION OF M. LUC RAINVILLE

SAMPLES		1	2	3	4	5	
		KRILL 15-11-01	KRILL 15-11-01	KRILL 15-11-01	KRILL 15-11-01	KRILL 15-11-01	
ANALYSIS							
ACIDITY (CITRIC ACID)	G/100G	0.02	0.03	0.03	0.03	0.03	0.03
INTERSPACE WATER	G/100G	9.48	9.43	9.61	16.95	11.48	
SULFITES	PPM	< 2	< 2	< 2	< 2	< 2	< 2
MOISTURE	G/100G	81.9	81.2	80.8	80.9	80.9	81.14
ASH	G/100G	3.0	2.9	3.0	3.0	3.0	2.78
PROTEINS	G/100G	13.2	13.6	13.6	14.2	14.1	13.77
FAT	G/100G	2.0	2.3	2.2	2.3	2.5	2.26
CARBOHYDRATES	G/100G	0.0	0.0	0.3	0.0	0.0	0.00
ENERGY PER 100 G	CALORIES	71	75	75	78	78	75.4

*J. Beaupré*

JACQUELINE BEAUPRÉ, SUPERVISEURE - CHIMIE  
neptuneCHEMmas  
FAX : 450-972-6351  
FAX: 450-979-0660

01 12 05

RÉVISION 1

RAPPORT D'ANALYSE

Date 25 Février 2002

No de lot 12-2-02

Nom du produit : Krill lyophilisé en poudre

Description : Poudre couleur rosée, forte odeur de poisson.

Conditions d'entreposage :

TESTS	METHODES	SPECIFICATIONS	RESULTATS
Humidité	O'Haus	< 5%	1.1%
Microbiologie			
Compte Total	U.S.P.		500/g
Levures	U.S.P.		< 100/g
Moisissures			< 10/g
Coliformes Totaux	A.P.H.A.		< 100/g
S. Aureus	A.P. H.A.		absence
E. Coli 0157	U.S.P.		absence
Salmonella sp.	U.S.P.		absence

Analyste : *Abraham Toub*

*Q*

**SGS**

SGS Laboratoires d'Analyses Agro-Alimentaires  
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**NEPTUNE TECHNOLOGIES & BIORESSOURCES INC.**  
**500, St-Martin ouest, bureau 550**  
**Laval, Québec**  
**H7M 3Y2**

**À L'ATTENTION DE MME. TINA SAMPALIS**

**DATE DE RÉCEPTION: 02-03-06**  
**NUMERO DE LABORATOIRE: 160083519**  
**NOMBRE D'ÉCHANTILLONS: 2**  
**DATE DE RAPPORT: 02 03 26**  
**PAGE: 7 DE 7**  
**DATE D'ANALYSE: 02-03-06**

**ÉCHANTILLONS:**

<b>1</b>	<b>2</b>
<b>A-SGS-1</b>	<b>LK-SGS-1</b>
<b>EXTRACTION #114, 44IÈME SÉCHAGE</b>	<b>KRILL LYO EN POUDRE, LOT: 180202</b>
<b>DU 14-02-2002, EMBALÉ LE 15-02-2002</b>	<b>POIDS NET 250G</b>

**MÉTHODE:**

<b>BACTÉRIES TOTALES /G</b>	<b>MFHPB-33</b>	<b>&lt;100</b>	<b>1,400</b>
<b>COLIFORMES TOTAUX /G</b>	<b>MFHPB-34</b>	<b>&lt;10</b>	<b>&lt;10</b>
<b>E.COLI /G</b>	<b>MFHPB-34</b>	<b>&lt;10</b>	<b>&lt;10</b>
<b>STAPH. AUREUS /G</b>	<b>MFHPB-21</b>	<b>&lt;10</b>	<b>&lt;10</b>
<b>LEVURES /G</b>	<b>MFHPB-22</b>	<b>&lt;10</b>	<b>&lt;10</b>
<b>MOISSISURES /G</b>	<b>MFHPB-22</b>	<b>&lt;10</b>	<b>&lt;10</b>
<b>SALMONELLES /G</b>	<b>MFHPB-20</b>	<b>NON DÉTECTÉE</b>	<b>NON DÉTECTÉE</b>
<b>PSEUDOMONAS SPP.</b>		<b>&lt;50</b>	<b>50</b>

**DANIÈLE LESSARD**  
**SUPERVISEURE DES SERVICES TECHNIQUES ET DU CQ**  
 neptuneMICmas  
 FAX: 450-972-6351

**02 03 26**

Le présent rapport a été émis par la Société conformément à ses Conditions Générales pour les prestations de services de contrôle et d'analyse (copie disponible sur demande) L'émission du présent rapport ne dispense pas les acheteurs ou les vendeurs d'exercer tous leurs droits et d'exécuter toutes leurs obligations liés au contrat de vente. Toute stipulation: contrares n'engagent pas la Société. La responsabilité de la Société relative au présent rapport est limitée à la négligence prouvée et n'excèdera en aucun cas dix fois le montant de honoraires ou de la commission. Sauf disposition spéciale, les échantillons, s'il en a été prélevés, ne seront pas conservés par la Société au delà d'une période de un mois.



SGS Agri-Food Testing Laboratories  
A Division of SGS Canada Inc.

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Pointe-Claire, Quebec  
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Fax (514) 630-6095

## RAPPORT D'ESSAIS

NEPTUNE TECHNOLOGIES & BIORESSOURCES INC.  
500, St-Martin ouest, bureau 550  
Laval, Québec  
H7M 3Y2

DATE DE RÉCEPTION: 02 03 06  
NUMERO DE LABORATOIRE: 160083519  
NOMBRE D'ÉCHANTILLONS: 2  
DATE DE RAPPORT: 02 03 26  
PAGE: 5 DE 7  
DATE D'ANALYSE: 02 03 11

À L'ATTENTION DE MME. TINA SAMPALIS

PRODUIT: CONCENTRÉ DE PROTÉINES A-SGS-1

	DESCRIPTION	CONTENU uMOL/gr	CONTENU mg/gr	%	DESCRIPTION	CONTENU uMOL/gr	CONTENU mg/gr	%	
1	TAURINE	81	10.1	2.15	21	ISOLEUCINE	161	21.1	4.48
2	AC. ASPARTIQUE	312	41.5	8.81	22	LEUCINE	269	35.3	7.49
3	HYDROXYPROLINE				23	AC. ARGININOSUCCINIQUE			
4	THRÉONINE	188	22.4	4.75	24	TYROSINE	131	23.7	5.04
5	SÉRINE	120	12.6	2.68	25	B-ALANINE			
6	ASPARAGINE				26	PHÉNYLALANINE	165	27.3	5.78
7	AC. GLUTAMIQUE	392	57.7	12.24	27	AC. B-AMINO-ISOBUTYRIQUE			
8	GLUTAMINE				28	HOMOCYSTINE			
9	SARCOSINE				29	AC. Y-AMINO BUTYRIQUE			
10	AC. AMINOADIPIQUE				30	ORNITINE	46	6.1	1.29
11	PROLINE	199	22.9	4.86	31	LYSINE	282	41.2	8.75
12	GLYCINE	329	24.7	5.24	32	1-MÉTHYLHISTIDINE			
13	ALANINE	282	25.1	5.33	33	HISTIDINE	69	10.7	2.27
14	CITRULLINE	1			34	3-MÉTHYLHISTIDINE			
15	AC. AMINO-n-BUTYRIQUE				35	CARNOSINE			
16	VALINE	211	24.7	5.24	36	ARGININE	218	38.0	8.06
17	CYSTINE	30	7.2	1.53	37	TRYPTOPHANE	34	6.9	1.47
18	MÉTHIONINE	80	11.9	2.53					
19	HOMOCITRULLINE								
20	CYSTATHIONINE								
	Total	3600	471.3	100.0					

*J. Beaupré*

JACQUELINE BEAUPRÉ, SUPERVEISEURE - CHIMIE  
neptuneCHEMmas  
FAX: 450-972-5351

02 03 26

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185 boul. Brunswick  
Pointe-Claire, Québec  
Canada H9R 4Z1  
Téléphone (514) 630-6093  
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## RAPPORT D'ESSAIS

**NEPTUNE TECHNOLOGIES & BIORESSOURCES INC.**  
**500, St-Martin ouest, bureau 550**  
**Laval, Québec**  
**H7M 3Y2**

**DATE DE RÉCEPTION: 02 03 06**  
**NUMERO DE LABORATOIRE: 160083519**  
**NOMBRE D'ÉCHANTILLONS: 2**  
**DATE DE RAPPORT: 02 03 26**  
**PAGE: 4 DE 7**  
**DATE D'ANALYSE: 02 03 11**

À L'ATTENTION DE MME. TINA SAMPALIS

ÉCHANTILLONS	SPECIFICATIONS	<sup>1</sup>	<sup>2</sup>
		CONCENTRÉ DE PROTÉINES A-SGS-1	CONCENTRÉ DE PROTÉINES LK-SGS-1
ANALYSES			
ALUMINIUM	PPM	46	43
BARIUM	PPM	5.0	4.6
BORON	PPM	21	18
CADMIUM	PPM	0.6	0.4
CALCIUM	PPM	22600	17300
CHROMIUM	PPM	1.1	1.2
COPPER	PPM	114	92.2
FLUORIDE	PPM	376	411
IRON	PPM	54.6	45.2
LEAD	PPM	< 1	< 1
MAGNESIUM	PPM	6940	5010
MANGANESE	PPM	2.8	2.2
MERCURY	PPM	< 0.1	< 0.1
PHOSPHORUS	PPM	15200	13500
POTASSIUM	PPM	8290	14010
SELENIUM	PPM	5.2	4.4
SODIUM	PPM	19600	29300
STRONTIUM	PPM	346	260
SULPHUR	PPM	12600	11500
ZINC	PPM	74	53



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02 03 26

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 500, St-Martin ouest, bureau 550  
 Laval, Québec  
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 NUMERO DE LABORATOIRE: 160083519  
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 DATE DE RAPPORT: 02 03 26  
 PAGE: 2 DE 7  
 DATE D'ANALYSE: 02 03 11

À L'ATTENTION DE MME. TINA SAMPALIS

ÉCHANTILLONS	SPECIFICATIONS	1	2
		CONCENTRÉ DE PROTÉINES A-SGS-1	CONCENTRÉ DE PROTÉINES LK-SGS-1
ANALYSES			
CHOLESTEROL	MG/100G	26	528
SATURATED FATTY ACIDS	G/100G	0.42	1.93
MONOUNSATURATED	G/100G	0.38	1.68
POLYUNSATURATED	G/100G	0.33	1.95
TRANS	G/100G	< 0.01	< 0.01
EPA	G/100G	0.15	0.99
DHA	G/100G	0.14	0.62
PC	G/100G	0.31	3.32
PI	G/100G	0.04	0.04
PS	G/100G	0.05	0.07
PE	G/100G	0.16	0.58
SM	G/100G	0.05	0.16

JACQUELINE BEAUPRÉ, SUPERVISEURE - CHIMIE  
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02 03 26



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## RAPPORT D'ESSAIS

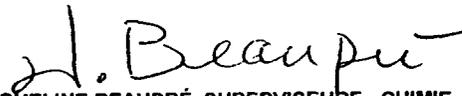
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500, St-Martin ouest, bureau 550  
Laval, Québec  
H7M 3Y2

DATE DE RÉCEPTION: 02 03 06  
NUMERO DE LABORATOIRE: 160083519  
NOMBRE D'ÉCHANTILLONS: 2  
DATE DE RAPPORT: 02 03 26  
PAGE: 1 DE 7  
DATE D'ANALYSE: 02 03 11

À L'ATTENTION DE MME. TINA SAMPALIS

ANALYSES	ÉCHANTILLONS	SPECIFICATIONS	1	2
			CONCENTRÉ DE PROTÉINES A-SGS-1	CONCENTRÉ DE PROTÉINES LK-SGS-1
MOISTURE	G/100G		2.76	2.92
FAT	G/100G		1.13	5.54
PROTEIN	G/100G		81.71	73.39
ASH	G/100G		14.07	15.77
CARBOHYDRATES	G/100G		0.33	2.38
ENERGY	CAL/100G		338	353
ENERGY	KJ/100G		1436	1493
OXYCAROTENOIDS*	MG/100G		0.7	11.0
ACETONE	PPM		300	--

\* Astaxanthine & canthaxanthine

  
JACQUELINE BEAUPRÉ, SUPERVISEURE - CHIMIE  
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02 03 26



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## RAPPORT D'ESSAIS

NEPTUNE TECHNOLOGIES & BIORESSOURCES INC.  
500, St-Martin ouest, bureau 550  
Laval, Québec  
H7M 3Y2

DATE DE RÉCEPTION: 02 03 08  
NUMERO DE LABORATOIRE: 160083519R  
NOMBRE D'ÉCHANTILLONS: 2  
DATE DE RAPPORT: 02 05 08  
PAGE: 3 DE 7  
DATE D'ANALYSE: 02 03 11

À L'ATTENTION DE MME. TINA SAMPALIS

ÉCHANTILLONS	SPECIFICATIONS	1	2
		CONCENTRÉ DE PROTÉINES A-SGS-1	CONCENTRÉ DE PROTÉINES LK-SGS-1
ANALYSES			
VITAMIN A (RETINOL)	UI/100G	275	7100
VITAMIN E	UI/100G	16	62
VITAMIN D	UI/100G	<10	<10
RIBOFLAVIN (B2)	MG/100G	6.6	23.6
THIAMINE (B1)	MG/100G	< 1	< 1
VITAMIN H6	MG/100G	< 0.1	< 0.1
CYANOCOBALAMINE (B12)	UG/100G	< 10	< 10
FOLIC ACID	MG/100G	0.2	1.7
PANTHOTENIC ACID	MG/100G	102	676
BIOTIN	PPM	92	<10
NIACIN	MG/100G	67.6	187.3

MILLIE CHEN  
COORDONNATRICE DE LABORATOIRE  
neptuneCHEMmas  
FAX: 450-972-6351

02 05 08

Révision 2

Le présent rapport a été émis par la Société conformément à ses Conditions Générales pour les prestations de services de contrôle et d'analyse (copie disponible sur demande). L'émission du présent rapport ne dispense pas les acheteurs ou les vendeurs d'exercer tous leurs droits et d'acquiescer toutes leurs obligations liées au contrat de vente. Toute stipulation contraire n'engage pas la Société. La responsabilité de la Société relative au présent rapport est limitée à la négligence prouvée et n'excède en aucun cas dix fois le montant des honoraires ou de la commission. Sauf disposition spéciale, les échantillons, s'il en a été prélevés, ne seront pas conservés par la Société au-delà d'une période de un mois.



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## RAPPORT D'ESSAIS

NEPTUNE TECHNOLOGIES & BIORESSOURCES INC.  
600, St-Martin ouest, bureau 550  
Laval, Québec  
H7M 3Y2

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IRON	PPM	54.6	45.2
LEAD	PPM	< 1	< 1
MAGNESIUM	PPM	6940	5010
MANGANESE	PPM	2.8	2.2
MERCURY	PPM	< 0.1	< 0.1
PHOSPHORUS	PPM	15200	13500
POTASSIUM	PPM	8290	14010
SELENIUM	PPM	5.2	4.4
SODIUM	PPM	19600	29300
STRONTIUM	PPM	346	260
SULPHUR	PPM	12600	11500
ZINC	PPM	74	53

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**Aquasearch, Inc.****Technical Report**

## ***Haematococcus Pluvialis and Astaxanthin Safety For Human Consumption***

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Safety for human consumption of *Haematococcus pluvialis* algal meal and astaxanthin has been demonstrated by a number of studies:

- A recent 28-day rat study with *Haematococcus pluvialis* dry algal meal, produced by Aquasearch's proprietary technology, demonstrated that there was no observed sub-acute toxicity at a daily dose of 50 mg/kg body weight, corresponding to 3,500 mg algal meal per 70-kg body weight of a typical adult man.
- No lethality was seen for *Haematococcus pluvialis* algae at doses up to 5000 mg/kg body weight, in an earlier, 13-day, single-dose (acute-toxicity), rat study.
- A human safety study demonstrated that daily ingestion of up to 1,140 mg Aquasearch's *Haematococcus pluvialis* algal meal, for 29 days, did not result in any safety concern.
- A recent sub-acute rat toxicity with Aquasearch's *Haematococcus pluvialis* algal meal, showed no signs of toxicity, after dosing rats with up to 1.15 mg astaxanthin per kg body weight per day (equivalent to 80.5 mg astaxanthin per 70-kg body weight) for 28 consecutive days.
- In a human safety study with Aquasearch's algal astaxanthin, no sign of toxicity or safety concern was observed, when volunteers ingested up to 19.25 mg astaxanthin per day for 29 days, while an earlier human study failed to find any harmful effect from 14.4 mg/day astaxanthin ingestion for two weeks.
- Pure astaxanthin (up to 80 mg/kg feed), is Generally Considered As Safe by FDA, for use in salmon diets. This can result in astaxanthin deposition of 10 to 15 mg/kg in salmon fillets. Levels of astaxanthin naturally occurring in wild-caught seafood, and dietary studies on carotenoids, seafood, and salmon,

also suggest that a daily serving of 5 mg astaxanthin, corresponding to 125 g of wild-caught Sockeye salmon fillet or less than 100 g of krill, is safe.

- The proprietary technology and quality control developed by Aquasearch to produce *Haematococcus pluvialis* algal meal, ensure that the product meets dietary supplement safety standards.

**Conclusion: A supplement containing 5 mg astaxanthin derived from 250 mg, or less, of Aquasearch's *Haematococcus pluvialis* algal meal is safe for daily human consumption.**

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Aquasearch's proprietary technology allows the production of a high quality algal meal containing 2% total astaxanthin or more. It is therefore a very good source of natural astaxanthin, a carotenoid pigment and biological antioxidant widely encountered in nature. Safety for human consumption of astaxanthin and *Haematococcus pluvialis* algae has been demonstrated by a number of studies.

## 1. Toxicity studies

### 1.1. *Haematococcus* algae.

#### 1.1.1. Human safety study

In a recent clinical safety study with Aquasearch's *Haematococcus pluvialis* algal meal, 33 human volunteers (15 males and 18 females, age 28 to 62) ingested on a daily basis, for 29 consecutive days, either a Low Dose supplement containing 228 mg algal meal and 3.85 mg astaxanthin, or a High Dose supplement containing 1140 mg algal meal and 19.25 mg astaxanthin.<sup>1</sup>

Volunteers underwent a complete medical examination before, during and at the end of the study. The physician, examined specifically, but not exclusively, the weight, skin coloration, general appearance, blood pressure, vision and eye, (near and distant vision, color vision, depth perception, eye condition), ears and nose, mouth, throat and teeth, chest and lungs, and reflexes, for each volunteer.

This medical examination was complemented by extensive urine analyses and blood analyses (cell counts, hemoglobin, liver enzyme activity indicators, and other blood parameters) (Table 1). No ill effects or toxicity from ingestion of the supplement were

observed, confirming the absence of toxicity of Aquasearch's *Haematococcus pluvialis* algal meal.

### 1.1.2. Rat toxicity studies

Absence of toxicity of *Haematococcus pluvialis* has also been demonstrated in rats and mice, widely accepted animal models for safety assessment of human dietary supplements.

A 28-day sub-acute rat toxicity study, with *Haematococcus pluvialis* algal meal produced with Aquasearch's proprietary technology, failed to find any sign of toxicity of this algal meal.<sup>2</sup> Three groups of 20 rats each (10 males/10 females) were fed daily by gavage 0, 5, or 50 mg/kg algal meal in a corn oil suspension for 28 consecutive days (corresponding to daily doses of 0, 350 mg and 3,500 mg algal for 70-kg body weight). After sacrifice, the post-mortem observations, hematology and clinical chemistry failed to detect any sign of toxicity.

An earlier 13-day rat toxicity study demonstrated that the LD50 acute toxicity of *Haematococcus pluvialis* algal meal in rats was greater than 5000 mg/kg.<sup>3</sup> In this study, three separate groups of 10 rats (5 males and 5 females per group) were fed 5,000 mg/kg algal meal suspended in a 0.5% methylcellulose solution. Mortality, body weights, necropsy examination and pharmacotoxic signs were evaluated on each group. The study found no remarkable differences in body weights or visible abnormalities. The post-mortem examination after sacrificing the animals at the end of the study revealed no abnormalities.

Another acute toxicity trial was reported with male and female mice.<sup>4</sup> In this study, *Haematococcus pluvialis* algal meal was suspended in distilled water for gavage to give a 30% solution (w/v). The solution was given in a single dose, at dosages ranging from 10,417 to 18,000 mg/kg. No mortalities occurred and no abnormalities were observed in the post-mortem examination. When converted to a 70-kg body weight, these doses are equivalent to single doses ranging from 729 g to 1,260 g.

### 1.1.3. Other studies

In salmonids, numerous experiments have shown that *Haematococcus pluvialis* can be incorporated in the diet at dosages ranging from 0.1% to 6% without any negative effect on growth or survival.<sup>5,6,7,8</sup> A recent report showed no indication of disease, toxicity or neoplasia in fish fed *Haematococcus pluvialis* as a dietary source of astaxanthin.<sup>4</sup> The fish were reported in excellent nutritional status with abundant body fat. Studies have also

indicated that feeding *Haematococcus pluvialis* can enhance growth and/or survival in trout and shrimp.<sup>8-10</sup>

## **1.2. Astaxanthin.**

Astaxanthin naturally appears in the human diet when seafood such as salmon, red fishes, shrimp, krill or lobster are eaten.

### **1.2.1. Human studies**

The recent clinical safety study, mentioned above, proved the safety of astaxanthin from Aquasearch's *Haematococcus pluvialis* algal meal.<sup>1</sup> In that study, 33 human volunteers (15 males and 18 females, age 28 to 62) ingested on a daily basis, for 29 consecutive days, either 3.85 mg or 19.25 mg algal astaxanthin. As mentioned earlier, extensive blood and urine analyses were conducted throughout the study (Table 1), and the physician conducted a detailed medical examination. Based on the results of these urine and blood analyses and the observations of the physician, no sign of toxicity from astaxanthin was detected even at the higher dose.

In a study with healthy human patients, who ingested up to 14.4 mg/day astaxanthin for two weeks, no ill effect was reported.<sup>11</sup> On the contrary, a positive antioxidant effect of astaxanthin on serum Low Density Lipoprotein (LDL) was observed. In that study, thirteen healthy patients were selected, subdivided into 3 groups, and given three levels of astaxanthin daily, for two weeks, as follows: 5 patients fed 3.6 mg/day, 5 patients fed 7.2 mg/day, and 3 patients fed 14.4 mg/day. The astaxanthin was administered sublingually in the form of a softgel capsule. Blood samples were taken and the LDL fraction was collected and exposed to an oxidizing agent. The study demonstrated that increasing doses of astaxanthin significantly and increasingly slowed down the oxidation of the LDL fraction.

### **1.2.2. Rat toxicity studies**

In the recent study with Aquasearch's *Haematococcus pluvialis* algal meal, described above, rats ingested daily up to 1.15 mg astaxanthin per kg body weight (equivalent to 80.5 mg for 70-kg body weight per day), for 28 days, without showing any sub-acute toxicity sign.

Other animal studies on the effects of astaxanthin have shown that even higher doses could be fed to rats for prolonged periods. Some of these studies have demonstrated beneficial

results. In one study, feeding rats 500 ppm astaxanthin for 34 consecutive weeks resulted in reduced cancer occurrence in the intestinal and oral mucosa and improved the condition of the oral cavity.<sup>12,13</sup>

### 1.2.3. Safety of astaxanthin in food salmon – safe daily dose of astaxanthin

For years, astaxanthin has been added to aquaculture diets at levels of up to 200 mg/kg, without any toxic effect on target animals. Additionally, numerous studies have demonstrated improved growth, survival and immune response in fish and shrimp.<sup>8-10,14-23</sup> Astaxanthin is regularly added at 50 ppm or higher to commercial diets fed to food fish for prolonged periods, i. e., for up to 2 years in the case of farmed salmon.

According to the Code of Federal Regulations, astaxanthin is Generally Recognized As Safe ("GRAS") when used as a color additive in salmon foods, with a maximum inclusion of 80 mg/kg feed.<sup>24</sup> Numerous studies have shown that such an inclusion level results in accumulation of astaxanthin in the flesh of Atlantic salmon at levels between 4 and 10 mg/kg, and at even higher levels in other species (Table 2).

These levels in Atlantic salmon are comparable to or slightly higher than levels observed in their wild counterparts, but lower than levels found in other wild salmon species found on the Pacific coast of the United States, where values as high as 58 ppm in Sockeye salmon were reported by a recent FDA study.<sup>25</sup> (Average of astaxanthin measurements in this study were 13.8 ppm in Coho salmon and 40.4 ppm in Sockeye salmon).

It was noted that the main astaxanthin stereo isomer identified by the FDA researchers in the 5 species of wild Pacific salmon they studied, was the 3S,3'S stereo isomer, identical to that found in *Haematococcus pluvialis*.<sup>8,25</sup>

Salmon, a fish rich in omega-3 fatty acids, is considered a healthy food, and, like other sources of these poly-unsaturated fatty acids, is highly recommended by nutritionists.<sup>26-29</sup> According to an epidemiological study on Alaska's native and non-native residents, the lowest rate of ischaemic heart disease mortality, less than one-third that of US Caucasians, occurred in Alaskan Eskimos who lived in an area with documented patterns of high salmon consumption by individuals with high blood concentrations of omega-3 fatty acids.<sup>28</sup> Based on the salmon flesh astaxanthin values mentioned above, a daily consumption of a 200-g portion of wild Sockeye salmon with 40 ppm astaxanthin in the flesh would lead to a daily ingestion of 8 mg astaxanthin per day. From a different point of view, the intake of a 5 mg supplement of astaxanthin corresponds to eating 500 g per day

of farmed rainbow trout or Atlantic salmon, 125 g of wild Sockeye salmon, or less than 100 g of krill.

Based on these published data, as well as the animal toxicity data publicly available, it may be inferred that the ingestion of 5 mg astaxanthin per day by an adult human is reasonably safe. This was further substantiated by Aquasearch's 29-day human safety study, which investigated the safety of 3.8 mg astaxanthin/day and 19 mg/day astaxanthin from *Haematococcus pluvialis* algal meal, i. e., almost four-fold higher than the assumed safe daily dose of 5 mg.<sup>1</sup>

The results of the extensive blood and urine analyses and complete physical examinations before, during, and at the end of the trial period, raised no apparent safety concern. The data were reviewed by two independent physicians, a clinical pathologist and a professional pharmacotoxicologist, all of who concurred that both doses were safe.

## 2. Non-mutagenicity of *Haematococcus*

A recent study<sup>30</sup> reported no mutagenic effect of *Haematococcus pluvialis* algae, using a mutagenicity test with *Salmonella typhimurium* strains TA100, TA1535, TA98, TA1537, TA1538, and E.coli WP2 uvr A.

In this experiment, *Haematococcus pluvialis* algal meal was formulated in a 50mg/mL solution of dimethyl sulfoxide. The formulation was spread onto petri dishes in the presence of the microbial cultures with positive controls. The positive controls (mutagenic agents): 2-(2-furyl)-3-5(5-nitro-2-furyl)acrylamide, 1-ethyl-2-nitro-3-nitrosoguanidine, 9-aminoacridine, 2-aminoanthracene, and 2-nitrofluorene, showed a remarkable increase in the number of revertant colonies in every case, compared to the solvent control.

## 3. Carcinogenicity

*Haematococcus pluvialis* is not known to have any carcinogenic effect, or contain significant levels of recognized carcinogens. On the contrary, *Haematococcus pluvialis* contains a high level of astaxanthin which has widely demonstrated anticarcinogenic effects.<sup>31-35</sup>

## 4. Heavy metals

*Haematococcus pluvialis* algae produced and processed by Aquasearch for human food consumption meet the Federal Food and drug Administration's list of maximum tolerances:

- Heavy metals (as lead): < 10.0 ppm
- Mercury < 1.0 ppm
- Cadmium < 0.5 ppm
- Arsenic < 2.0 ppm
- Lead < 5.0 ppm

This has been confirmed by analyses of various batches (Lot HP980051<sup>36</sup> and Lot 990610Mix<sup>37</sup>, a blend resulting from combining five batches: Lots 990513A, 990518B, 990520A, 990524A, 990526A, and therefore, highly representative of the quality of *Haematococcus pluvialis* algal meal produced with Aquasearch's technology).

## 5. Bacteriology

Manufacturing process follows FDA GMP recommendations for food supplements to avoid spoilage and contamination of *Haematococcus pluvialis* algal meal by harmful micro-organisms or other types of contaminants.

During the processing, the algal biomass is mechanically cell-broken to ensure a thorough rupture of cell walls, undergoes a pasteurization process, and is dried to a moisture content less than 5%. The pasteurization treatment ensures that the following bacteriological specifications in the final product are achieved, as confirmed by analyses by an independent laboratory<sup>37</sup>:

- Total aerobic plate count <1,000 CFU
- Total coliforms <10/g
- *E. coli* <10/g
- *Salmonella* absence in 25 g

## 6. Other natural toxic compounds and toxicity risks

Aquasearch is not aware of any significant or detectable levels of known carcinogenic or toxic compounds in *Haematococcus pluvialis* algae that could have a negative effect on human health.

Analyses on the algae meal have demonstrated absence of mycotoxins, and especially of aflatoxins.<sup>36,37</sup>

*Haematococcus pluvialis* may contain small amounts of canthaxanthin, a carotenoid

pigment closely related to astaxanthin. Analyses have shown that canthaxanthin concentrations in *Haematococcus pluvialis* algal meal produced with Aquasearch proprietary technology are less than 2% of total astaxanthin concentration. Aquasearch's proprietary technology maximizes astaxanthin biosynthesis by *Haematococcus pluvialis* and in so doing also minimizes the relative proportion of other carotenoids (including canthaxanthin).

At the levels of canthaxanthin encountered in Aquasearch's algal meal, a daily dose of 5 mg algal astaxanthin as a supplement would entail also ingesting 0.1 mg canthaxanthin per day. Although canthaxanthin has been demonstrated to have positive metabolic effects such as an anticancer activity,<sup>38</sup> there has been reports that, at high doses for prolonged periods, it can have negative effects. One case of aplastic anemia associated with canthaxanthin ingested for tanning purposes, was reported a few years ago<sup>39</sup>. Others have reported the appearance of crystalline formations in the retina of some individuals who ingested up to 66 g cantaxanthin over 24 months (corresponding to an average daily ingestion of 90 mg cantaxanthin per day) for tanning purposes<sup>40</sup>. However, later it was demonstrated that these canthaxanthin deposits in the retina could be reversed<sup>39</sup>. In any case, the levels of canthaxanthin that would be ingested through a 5 mg astaxanthin dietary supplement formulated with Aquasearch's algal meal are nearly 1000-fold lower than the doses which were observed to cause canthaxanthin maculopathy. Therefore, they should represent no safety risk.

The rat toxicity and human studies which were conducted with Aquasearch's algal meal confirmed this. It should also be noted that FDA has approved canthaxanthin as a color additive in fish foods (up to 80 mg/kg feed, which can result in canthaxanthin deposition levels of 4 to 12 mg/kg fillet) and broiler diets, as well as in foods and drugs.<sup>41</sup> In foods, the limit authorized by FDA is 30 mg canthaxanthin per pound of solid food. The ingestion of 0.1 mg cantaxanthin in a dietary supplement containing 5 mg astaxanthin, is therefore well below the levels that would be encountered in foods that are considered safe by FDA.

## **7. Product specifications**

A detailed description of the manufacturing process and of the specifications of *Haematococcus pluvialis* for use in dietary supplements are reviewed in a separate technical report.<sup>42</sup>

## **8. Metabolic effects of astaxanthin**

Astaxanthin is a powerful natural antioxidant. There is a growing amount of scientific

evidence not only on the safety of astaxanthin for human consumption, but on the positive metabolic effects that it may have. These findings have been reviewed in detail in Aquasearch Technical Reports TR.3002.001<sup>43</sup> and TR.3003.001<sup>44</sup>.

## 9. Dietary studies - safe daily dose of algal astaxanthin

Astaxanthin appears to be absorbed in the blood in the same way as other carotenoids. Carotenoids are absorbed by passive diffusion through the intestinal mucosa after being emulsified and solubilized in lipid micelles which are incorporated into chylomicrons when exiting the intestinal mucosal cells.<sup>45</sup> They are transported in the blood after being transferred from the chylomicrons to lipoproteins.

In a recent human study, a single dose of 100 mg dietary astaxanthin was not found to have any negative effect and demonstrated that astaxanthin has a similar absorption pattern to other carotenoids.<sup>46</sup> Astaxanthin was measured in the blood plasma of 3 middle-aged male subjects after ingestion of a single dose of 100 mg astaxanthin. Astaxanthin was readily absorbed and transported by various lipoproteins: chylomicrons/Very Low Density Lipoproteins, High Density Lipoproteins and Low Density Lipoproteins.

Plasma levels of astaxanthin peaked at 1.2 mg/L (= 2 µmol/L) after 6 hours and progressively declined over the next 66 hours to a 0.2 mg/L level. These levels and duration are comparable to levels reported in the literature for other carotenoids.<sup>47-49</sup> Astaxanthin appears to be absorbed at a similar rate than beta-carotene which peaks in the serum after 6 to 9 h.<sup>49</sup> In mice, astaxanthin also appeared to be absorbed quite effectively, when compared to beta-carotene or lutein.<sup>49</sup>

The official recommended dietary intake for vitamin A is 1,000 retinol equivalents, for men, and 800 for women.<sup>51</sup> This corresponds to 6 µg (*micrograms*) beta-carotene or 12 µg of other pro-vitamin A carotenoids.<sup>51</sup> On the other hand, practical levels of carotenoid intake are significantly higher. Epidemiological studies in North Europe have found daily ingestion of carotenoids ranging from 2.9 to 7.6 mg/ (*milligrams*) per day,<sup>52-54</sup> while in the US, the level of carotenoids supplied by the "normal" diet is estimated to be 1.5 mg beta-carotene per day.<sup>51</sup>

The Alliance for Aging Research, a US Citizen Advocacy organization for research to improve the health and independence of older people, has recommended 10 to 30 mg beta-carotene per day for optimal health, and doses of 20 to 180 mg beta-carotene for

many years have been used to treat erythropoietic protoporphyria, with no evidence of toxicity and without development of abnormally-elevated blood vitamin A levels.<sup>51</sup> In addition it should be noted that astaxanthin, unlike other carotenoids such as beta-carotene, has no provitamin A activity;<sup>55,56</sup> therefore it represents a lower risk of hyper-vitaminosis A.

It may be argued that because astaxanthin is closely related to canthaxanthin it could also have similar toxic effects as those described above. However, the available data indicate that astaxanthin consumption at no greater than the recommended dose of 5 mg per day poses no safety risk:

- The proposed daily intake of astaxanthin (5 mg) is much lower than the levels of canthaxanthin which were found to have toxic effects (up to 90 mg average daily intake for 24 months).
- The human safety study conducted with Aquasearch's algal astaxanthin found no changes in vision or eye condition in the patients. Another good indicator, skin coloration, did not change throughout the Aquasearch safety study.
- The post-mortem examination of the animals in Aquasearch's rat toxicity study also failed to find any adverse effect of astaxanthin supplementation at the doses tested.
- Researchers at the University of Illinois also reported that, in an animal model (rats), astaxanthin, unlike canthaxanthin, did not form crystalline depositions in the eye.<sup>57</sup> Furthermore, they demonstrated that astaxanthin can have a beneficial role in the protection of the eyes from UV-light damage.

In conclusion, based on published studies (reviewed above), on natural levels of astaxanthin found in seafood, and on the results of the studies conducted by Aquasearch, it appears that the consumption by a healthy adult human of a daily dose of 5 mg astaxanthin, in the form of a supplement formulated with 250 mg (or less) *Haematococcus pluvialis* algal meal produced with Aquasearch's proprietary technology, represents no safety risk. This suggested dose is approximately four times lower than the high dose which was demonstrated to be safe by Aquasearch's safety study.

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**Table 1: List of analyses in human safety study conducted on Aquasearch's *Haematococcus pluvialis* algal meal.<sup>1</sup>**

**Blood chemistry analyses**

Serum glutamate pyruvate transaminase (SGPT)  
Lactate dehydrogenase (LDH)  
Glucose  
Total protein  
Total bilirubin  
Blood urea nitrogen (BUN)  
Creatinine  
Total cholesterol  
High-density lipoprotein (HDL) cholesterol  
Triglycerides  
Low-density lipoprotein (LDL) cholesterol (calculated)  
Albumin  
Globulin

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**Complete blood count (CBC)**

White blood count (WBC)  
Red blood count (RBC)  
Hemoglobine (HGB)  
Hematocrit (HCT)  
Mean corpuscular volume (MCV)  
Mean corpuscular hemoglobin (MCH)  
Mean corpuscular hemoglobin concentration (MCHC)  
Red cell distribution width (RDW)  
Platelet count  
Neutrophil (segs)  
Lymphocytes  
Monocytes  
Eosinophils  
Bsophils  
Red blood cell morphology  
Coagulation test (activated partial thromboplastin time, PTT)

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## Urinalysis tests

Color	pH
Appearance	Protein
Specific gravity	Glucose
Leukocyte esterase	Ketones
Nitrite	Urobilinogen
Blood	Bilirubin

**Table 2. Levels of of astaxanthin in selected types of seafoods<sup>8</sup>**

Seafood type	Astaxanthin		
	Content (mg/kg)	Free/esterified	Main isomer
Sockeye salmon	26-37	Free,esterified**	3 <i>S</i> ,3' <i>S</i>
Coho salmon	9-21	Free,esterified**	3 <i>S</i> ,3' <i>S</i>
Chum salmon	3-8	Free,esterified**	3 <i>S</i> ,3' <i>S</i>
Chinook salmon	8-9	Free,esterified**	3 <i>S</i> ,3' <i>S</i>
Pink salmon	4-6	Free,esterified**	3 <i>S</i> ,3' <i>S</i>
Atlantic salmon	3-11	Free,esterified**	3 <i>S</i> ,3' <i>S</i>
Rainbow trout	1-3	Free,esterified**	3 <i>S</i> ,3' <i>S</i>
salmon eggs	0-14	Esterified***	N.A.
Red seabream	2-14	Esterified***	N.A.
Red seabream eggs	3-8	N.A.	N.A.
<i>Peneaus monodon</i>	10-150	Esterified,free**	3 <i>S</i> ,3' <i>S</i>
Lobster		Esterified,free**	N.A.*
Krill	46-130	Esterified***	3 <i>R</i> ,3' <i>R</i>
Krill oil	727	Esterified***	3 <i>R</i> ,3' <i>R</i>
Crayfish meal	137	Esterified***	N.A.*
Artic shrimp	1160	Esterified***	3 <i>S</i> ,3' <i>S</i>
<i>Haematococcus pluvialis</i>	10,000-30,000	Esterified***	3 <i>S</i> ,3' <i>S</i>

- \* Most crustaceans studied appear to have mostly the 3*S*,3'*S* form, unlike Krill.
- \*\* depending on tissues, free or esterified astaxanthin may be found
- \*\*\* also contain a small proportion of free astaxanthin

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[Return to Clinical Safety Study](#)



## **KOREA FOOD & DRUG ADMINISTRATION**

**SUBJECT : REGARDING KRILL PRODUCT**

**QUESTION FROM SAM OH**

**: THERE IS EPA AND/OR DHA FOOD IN HEALTH FOOD CATERGORIES AND, ITS DEFINITION IS 'A THINGS FROM EDIABLE FISHES, AQUATIC ANIMALS AND ALGAE;**

**WE HAVE A KRILL OIL (OMEGA 3 FATTY ACIDS (EPA/DHA) CONTENT 40% UP) AND, WE WOULD LIKE TO KNOW WHETHER THIS KRILL OIL IS EPA AND/ OR DHA FOOD. PLEASE INVESTIGATE AND LET US KNOW YOUR RESULT.**

**ANSWER FROM FOOD EVALUATION DEPARTMENT**

**: KRILL PRODUCT IS ACCEPTABLE AS A RAW MATERIAL FOR HEALTH FOOD BECAUSE IT IS CLASSIFIED INTO EDIABLE MATERIAL AND, KRILL OIL IS ALSO ACCEPTABLE AS EPA/DHA FOOD YOU CAN MEET THE KOREA FOOD CODE.**

# 식품의약품안전청

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제목 크릴새우에 대한 결의회신

1. 사이버민원 9125호(2002. 2. 2)와 관련입니다.
2. 현재 크릴새우는 식용가능한 식품원료로 분류되어 있으므로 건강보조식품의 원료로 사용가능하다고 판단되며, 질의하신 제품이 크릴새우에서 채취한 EPA/DHA 등의 지방산을 함유한 유지질 식용에 적합하도록 정제한 것 또는 이를 주원료로 하여 성취가 용이하도록 액상, 페이스트 상, 분말, 과립, 정제 또는 캡슐로 가공한 것이고, 식품공전상 기준·규격에 적합하다면 EPA/DHA 함유식품으로 분류될 수 있습니다. 끝.

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