CORNUCOPIA
INSTITUTE

November 13, 2011

Dear members of the National Organic Standards Board,

Enclosed, please find our analysis of the Martek petitions for their nutritional oils (some processed with the solvent hexane and formulated with a myriad of synthetic and non-organic ingredients).

The petitions by Martek Biosciences Corporation to include "DHA Algal Oil" and "ARA Single-Cell Oil" on the National List of Approved Substances (205.605) should be rejected.

The Technical Review (TR), which the Handling Committee used to write its recommendation, is a deficient, incomplete document (not conforming to the requirements set forth in the procedure manual) and failed to address several important issues.

The writers of the TR failed to fact-check several Martek claims, especially that all n-hexane is recycled and reused, that the microorganisms used are not genetically modified (any method of genetic modification that cannot occur under natural processes is prohibited in organics) and that the supplementation of foods with Martek's oil has been proven to be beneficial. As a result, the Handling Committee members made their recommendation based on incomplete and incorrect information from the TR.

We present the information in this packet to you to ensure that your decision is based on a thorough understanding of all the facts and on sound science, in addition to organic consumer surveys rather than conjecture and opinion.

We are confident that if you review this information, you will reach the conclusion that the Martek oils are not only inappropriate but also illegal in organics, and would do serious harm to the reputation of the organic label if approved.

Please feel free to contact me directly, via phone or e-mail, if you have any questions or would like to access the original research we referenced in this report.

Sincerely,

Charlotte Vallaeys
Director, Farm and Food Policy
The Cornucopia Institute
978-369-6409
vallaeys@cornucopia.org

CORNUCOPIA INSTITUTE

Comments on Martek Biosciences Corporation's Petition to include DHA Algal Oil and ARA Single-Cell Oil on the National List of Approved Substances

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Executive Summary

Mutated Algae (Genetically Modified)

(Appendix A)

GMOs are explicitly prohibited in organics, and are not eligible for consideration on the National List (7CFR205.105(e)).

The TR failed to address the origin of the strain of algae and fungus used for Martek's DHA and ARA oils.

Our research indicates that Martek Biosciences Corporation, which is a biotechnology company that uses various methods of genetic engineering to influence oil production by microorganisms, markets DHA oil from strains that have been genetically modified through mutagenesis. In fact, one of the strains was developed by Monsanto Corporation, and eventually acquired by Martek.

We thoroughly researched patents filed by Martek Biosciences Corporation with the US Patent Office, and they reveal that Martek is actively involved in genetic modification of algae and fungus, through recombinant DNA technology and other techniques.

Hexane

(Appendix B)

Hexane is classified by the Environmental Protection Agency (EPA) as a Hazardous Air Pollutant.

Factories and food processing plants that emit hexane into the air are required to report their emissions to the EPA. EPA data show that Martek's plant in South Carolina is among the top 100 emitters of hexane in the country – with 8,400 pounds of hexane released into the air in 2010.

In 2003, the State Fire Marshal of Kentucky linked an explosion at a wastewater treatment plant to hexane emissions from Martek's Winchester, KY plant (hexane is a highly explosive, Class I flammable liquid).

The TR failed to fact-check Martek's claim that all hexane they use is "recycled and reused." The correct answer to the question, "are there adverse effects on the environment from manufacture" should be "yes."

Moreover, little is known about long-term effects of consuming foods immersed in n-hexane, which is a neurotoxin. The FDA does not require testing for residues, and does not set a maximum residue level in foods processed with this petrochemical.

Synthetic Ingredients
(Appendix C)

Martek's oils and powders contain numerous synthetic and non-organic ingredients that have not been approved for use in organics.

Synthetics that were in fact identified in the Martek petition were not analyzed in the TR. Moreover, Martek uses non-organic sunflower oil in its oils, and neither the TR nor the Handling Committee has raised the specific question of whether this oil is hexane-extracted, how much is present in the final product, and the general question of why Martek would be allowed to use non-organic agricultural ingredients that are not listed on 205.606.

More troubling is Martek's failure to disclose numerous synthetics used in its production of "Life'sDHA" products. For example, "DHA Algal Oil Powder" in HappyBellies™ certified organic baby cereal contains mannitol (an unapproved sugar alcohol), sodium polyphosphate (an unapproved synthetic), modified starch (unapproved non-agricultural product, possibly from GMO corn) and glucose syrup solids (unapproved non-agricultural product, possibly from GMO corn).

Without a clear understanding of the full spectrum of synthetics used in its formulated products, and without the commitment by Martek to use organic agricultural products in its oils, the Martek petitions should be rejected.

Natural Alternatives Exist
(Appendix D)

In determining whether Martek's oils are *essential* in organic handling, Board members cannot ignore the fact that organic manufacturers, who wished to avoid Martek's unapproved oils, have turned to fish oil and egg phospholipids as sources of DHA.

Fish oil has been added to certified organic milk (Organic Valley), yogurt (Stonyfield) and baby food (Gerber) as a source of DHA. A blind taste test of milk with fish oil revealed that no taster was able to identify a "fishy" flavor. Fish oil, which is not hexane-extracted, has appeared on the National List since 2007, with the important annotation that only organic stabilizers, or stabilizers on the National List, may be used.

In baby formula, a certified organic manufacturer has added egg phospholipids as a source of DHA and ARA – offering organic parents an alternative to formula with Martek's hexane-extracted algae and fungus.

Not Essential in Organic Handling
(Appendix E)

Martek's oils are not essential in organic handling. Organic products can be made without these oils, and organic and natural alternatives exist. Moreover, if an organic consumer wishes to supplement with DHA, they can buy supplements. Supplements are available for every segment of the population, from the general adult population (in the form of pills) to pregnant and nursing mothers (in the form of prenatal supplements) to children (in the form of "chewables") to infants (in the form of a liquid that can be added to formula or milk). Supplements derived from fish oil and from Martek's algal oil are available, offering consumers a wide range of DHA supplements.

The Handling Committee answered "N/A" to the question of essentiality in organic handling. The "N/A" category is for questions that do not apply to the material; for example, "Are there detrimental physiological effects on soil organisms, crops, or livestock?" is not relevant for the Martek oils, and "N/A" is an appropriate answer. But for the question, "is the substance essential for handling?" the question must be answered and cannot be ignored. The correct answer is "no," DHA algal oil is <u>not</u> essential for handling.

Organic Consumers Reject Martek's Oils
(Appendix F)

According to a poll of nearly 1,500 organic consumers, conducted by PCC Natural Markets, the largest food cooperative in the United States with 9 stores in the Seattle area, the overwhelming majority of shoppers would reject organic products with Martek's oils if they knew the details of the sourcing of the microorganisms and processing methods used by Martek.

76.4% of shoppers polled in the PCC survey would not purchase organic products with DHA from genetically modified algae, and 88.6% would not purchase organic products with hexane-extracted DHA oil. If consumers knew that Martek's oils are stabilized with synthetic ingredients, the PCC poll suggests that 78.3% of consumers would not purchase the products (current ingredient lists simply state "DHA Algal Oil" without disclosing the ingredients in the oil, which includes synthetics).

Meanwhile, 56.2% of consumers would be more inclined to purchase organic products if they contained DHA from wild fish, and 51.6% would be more inclined to purchase organic products if they contained DHA from organic algae.

Additional Concerns
(Appendix G)

We raised several additional concerns with the Handling Committee's recommendation, including its disregard of evidence and studies showing potential harm of DHA supplementation. First, it represents extreme bias, by the Handling Committee, to accept studies done with fish oil showing benefits of omega-3 consumption, and assume this means the same benefits exist with isolated DHA consumption (Martek's patented product), but ignore the studies showing potential adverse effects, including from oversupplementation, because they were done with fish oil.

We are also concerned that Martek Biosciences Corporation has not performed adequate post-market surveillance and safety studies to ensure its oils are well tolerated by infants (as recommended by the FDA as part of the GRAS system). We present a representative sampling of reports, which were submitted to the FDA by healthcare professionals and parents, indicating that at least a subset infants experience serious gastrointestinal reactions from Martek's oils.

Problems with the Technical Review
(Appendix H)

The NOSB's Policy Manual lists specific quality criteria that Technical Review must meet. The TR for DHA Algal Oil fails the majority of these criteria, including the requirements to be consistent, to be free from opinion and conjecture (statements not backed up by documented research), to be based on the best available information, and to be thoroughly supported using literature citations. These shortcomings are detailed in Appendix H.

Most egregiously, the TR merely parrots <u>many</u> of Martek's claims without verifying them. In some instances, the TR does verify a claim independently, but additionally includes misleading conjecture. For example, the TR includes the following unreferenced sentence: "Supplementation with omega-3 fatty acids such as DHA could potentially help prevent or treat neurological disorders associated with memory loss, like Alzheimer's disease." The TR then attempts to verify this claim, and finds the following study (the abstract of this study is included in this packet): "A placebo-controlled trial with 295 patients with Alzheimer's disease found that DHA supplementation (2 grams/day) for 18 months was **<u>not</u>** effective in slowing cognitive decline." (TR 508-515) An unbiased TR with requisite scientific integrity would not have included the conjecture ("could potentially help treat") and simply state the study findings: "DHA supplementation was not effective in slowing cognitive decline."

Appendix A

Mutated Algae and Fungal Oils

GMOs are explicitly prohibited in organics, and are not eligible for consideration on the National List (7CFR205.105(e)).

Martek Biosciences Corporation is a biotechnology company that genetically engineers algal and fungal microorganisms for high DHA and ARA production. The company, now owned by the multi-billion dollar, multinational corporation DSM (based in The Netherlands), is currently using recombinant DNA technologies on organisms in an attempt to make algae produce EPA, another long-chain omega-3 fatty acid found in fish oil, in addition to DHA (see US Patent 7,973,149).

The strain of algae that Martek currently uses to produce one type of its DHA Algal Oils was developed in Monsanto's laboratories through "classical mutagenesis," which entails blasting algal microorganisms with chemicals or radiation to artificially induce genetic mutations, and screening the organisms until one with a favorable genetic mutation – in this case, high DHA production – is identified.

***Consumer Acceptance of Martek's Oils**:* According to a consumer poll by PCC Natural Markets, which surveyed nearly 1,500 organic consumers, 76.4% "would not purchase" organic products supplemented with genetically engineered algae, and 12% would be "less inclined to purchase" these products. Only 2.3% of organic shoppers would be "more inclined" to purchase organic products with genetically modified algae.

These findings indicate that many organic consumers who are currently purchasing products with Martek's algal oil would not have made these purchases if they knew the full story behind the algal oil. Current sales of organic products with Martek's oils are likely the result of misled consumers, who believed they were purchasing a truly organic product containing only organic and approved ingredients.

***Organic Standards Prohibit Martek's Oils**:* The organic standards prohibit genetic modification of organisms. 7CFR205.105(e) states that "To be sold or labeled as "100 percent organic," "organic," or "made with organic (specified ingredients or food group(s))," the product must be produced and handled without the use of: (e) excluded methods," which refers to genetic modification.

The standards clearly state that "excluded methods" are not restricted to recombinant DNA technology, but include other methods that "genetically modify organisms or influence their growth and development by means that are not possible under natural conditions" (7CFR205.105(e)).

"Classical mutagenesis" is not specifically listed as an excluded method, but mutations through harsh chemicals or radiation do not occur "under natural conditions" and should therefore be prohibited from organics.

***Incomplete Technical Review**:* The Technical Review, which was deficient in several respects, failed to include this information. The Handling Committee's recommendation was therefore based on incomplete information.

Since Genetically Modified Organisms (GMOs) (which definition is not limited to genetically modified organisms using recombinant DNA technology) are not eligible for consideration on the National List, the Board should vote to reject the Martek DHA Algal Oil petition.

DSM position on biotechnology

Key messages

Biotechnology is a very promising field, offering substantial benefits in the areas of health, nutrition and the environment. Widespread application of biotechnology is a critical factor in ensuring health and prosperity for mankind and making the world more sustainable.

Biotechnology in its modern form opens up opportunities to produce unique, high-value compounds in applications varying from pharmaceuticals to personal care products, healthy ingredients for food or feed, bio-based chemicals and materials as well as biofuels from renewable resources.

In using biotechnology, DSM adheres to all applicable regulations and legislation and applies the highest standards. We are transparent about the technologies we use in our products.

Introduction
We believe that biotechnology offers unique solutions to global challenges related to a growing and aging population and the depletion of fossil resources. This paper outlines the development of biotechnology, its promise for improving the quality of life, its future role in the global economy, and its relation to issues concerning sustainability and human ethics. It also outlines how DSM uses biotechnology to achieve its mission.

What is biotechnology?
Biotechnology is a field of applied biology that involves the use of cells and proteins (including enzymes) derived from these cells in bioprocesses for a broad range of applications like pharmaceuticals, food, agricultural products, bio-based chemicals and materials as well as fuels. Generally, bioprocesses use renewable resources as starting material and are operated at mild conditions (e.g. using water instead of organic solvents and at low pressures and temperatures) in an environmentally responsible way. Quite often biotechnology offers the opportunity to make compounds that cannot be made in any other way.

Many biotechnological techniques (e.g., selective breeding to optimize crops and livestock, and fermentation to produce bread, cheese, beer, wine and yoghurt) have been in use since antiquity. In the late 19th century, these biotechnological processes began to be industrialized. In 1953, the discovery of the structure of DNA and the mechanism by which genetic information is passed on gave rise to the sub-discipline of biotechnology known as genetic engineering. Genetic engineering is the direct and controlled modification of genes, cells and living tissue to bring about changes in the genetic make-up of an organism. Combined with advances in other fields, these techniques have opened up the possibility of totally new applications of biotechnology.

Today, modern biotechnological techniques are used to produce bio-based materials and ingredients and intermediate products with more precise specifications and in many cases to higher standards than other processes currently would allow. These techniques often enable products to be manufactured more efficiently at lower cost, using less energy or smaller quantities of raw materials and producing far less waste.

DSM and biotechnology

DSM is a global leader in biotechnology and is widely recognized for its innovations in bioproducts, enzyme solutions and services. DSM's involvement with biotechnology dates back to 1870 (see annex 1). We have a broad expertise in biotechnology (see annex 2) and chemical manufacturing, combined with in-depth knowledge of a wide variety of end-user markets from food and pharma to chemicals and materials. This puts DSM in a unique position to identify, develop and scale-up commercially viable biotechnological innovations. Our biotechnological processes are well-contained and meet the highest safety standards. The well-being of humans and animals and the quality of our environment are the major concerns of any company, and this certainly holds true for DSM.

Biotechnology helps us to achieve our mission to create brighter lives for people today and generations to come through solutions that nourish, protect and improve performance. We pursue this mission

- in the Materials Sciences field, with products for the automotive industry, coatings and paints, electrical and electronic components, life protection equipment and construction materials;
- in the field of the Life Sciences, with products relating to human and animal nutrition, pharmaceuticals, health and personal care;
- at the crossroads of Materials Sciences and Life Sciences, with products related to bio-based building blocks and biomedical materials.

Many of these products can be produced with the aid of micro-organisms (either in their natural state or optimized using modern biotechnology), resulting in better properties and environmentally friendlier processes, or a combination of these. Increasingly, we are combining the techniques of biotechnology with chemistry to achieve the best possible results for our customers and the environment.

Biotechnology and sustainability

We take a broad view of sustainability – one in which social responsibility, environmental quality and economic performance go together. We believe that innovative applications of biotechnology will play a key role in advancing sustainability in the coming decades. They will, for instance, help reduce the world's reliance on fossil resources by making the production of biofuels and chemicals more efficient and sustainable. And by improving crop yields and quality, biotechnology will also help improve the output of agriculture. In short, biotechnology will be fundamental to the world's transition to a bio-based economy.

The bio-based economy

While biotechnology is already very much part of everyone's daily life, it is set to play an even larger part in the future. We are now facing a number of fundamental global challenges like the rapidly increasing consumption, the effects of climate change, the increasing costs of fossil-resources and ultimately even the availability of these resources. In the future, we will need to go back to living off the land, just as our ancestors did. Biotechnology will allow us to produce from plant-materials, both, human food, by extracting nutritional high quality human food proteins, as well as biochemicals and biofuels. This shift to a bio-based economy will be the turning point towards the next – green – industrial revolution to secure our food, chemicals and fuel needs in the future.

What will this emerging bio-based economy look like? For a start, we will see the development of new and more sustainable processes and products, as we learn more about genes and complex cell processes. It is generally believed that biotechnology will make its mark in the following areas:

- Agriculture (especially in plant and animal breeding)
- Human health (diagnostics, therapeutics, (bio)pharmaceuticals, functional foods, and medical devices)
- The chemical industry (enzymes, bio-based chemicals, plastics and fuels; cleaner chemical processes)

The potential economic and environmental benefits of biotechnology have created a growing strategic interest in the bio-based economy in many parts of the world, and indeed, such an economy will inevitably be global. As the OECD pointed out in a recent report, the nations of the developed world will not be the only ones to benefit: biotechnological applications to restore or improve environmental conditions and to improve crop yields will be particularly relevant to less developed countries.

Dialogue with society

New or unfamiliar technologies often raise concerns in society about their possible implications for public health, the environment, or trigger ethical discussions. Biotechnology is no exception – particularly when it involves genetic engineering. DSM fully recognizes these concerns and believes in engaging in an open dialogue and debate on benefits and risks with all stakeholders, including the scientific community, industry, NGOs, governments and the general public.

Examples of this dialogue are the discussions we engage in with (national) authorities on upcoming legislation or changes in existing legislation on e.g. GMOs, the open days that we organize to allow the general public (site neighbors, schoolchildren, etc.) to visit our R&D and production facilities, and the courses on modern biotechnology we organize for laymen.

In order to enable the competent authorities to assess and accept our use of innovative strain development technologies and the resulting genetically modified production micro-organisms, we are transparent about our practices and use science-based safety assessments. Moreover, in our biotechnology operations we apply best industry practices in accordance with the most recent insights.

Conclusion

In summary, we believe that biotechnology will have an increasingly important role to play in making the world more sustainable, in improving human and animal health, and in raising the quality of life for millions of people around the world. As a global leader with a broad range of expertise, and fully conscious of our social responsibility, we are ready to play a full part in exploring this future – safely and creatively.

United States Patent **7,973,149**
Metz , et al. **July 5, 2011**

PUFA polyketide synthase systems and uses thereof

Abstract

The invention generally relates to polyunsaturated fatty acid (PUFA) polyketide synthase (PKS) systems isolated from or derived from non-bacterial organisms, to homologues thereof, to isolated nucleic acid molecules and recombinant nucleic acid molecules encoding biologically active domains of such a PUFA PKS system, to genetically modified organisms comprising PUFA PKS systems, to methods of making and using such systems for the production of bioactive molecules of interest, and to novel methods for identifying new bacterial and non-bacterial microorganisms having such a PUFA PKS system.

Inventors: **Metz; James G.** (Longmont, CO)**, Flatt; James H.** (Colorado Springs, CO)**, Kuner; Jerry M.** (Longmont, CO)**, Barclay; William R.** (Boulder, CO)
Assignee: **Martek Biosciences Corporation** (Columbia, MD)
Appl. No.: **11/777,278**
Filed: **July 12, 2007**

Related U.S. Patent Documents

Application Number	Filing Date	Patent Number	Issue Date
10124800	Apr., 2002	7247461	
09231899	May., 2003	6566583	
60284066	Apr., 2001		
60298796	Jun., 2001		
60323269	Sep., 2001		

Current U.S. Class: **536/23.1** ; 435/134; 435/252.1; 800/280; 800/295
Current International Class: C07H 21/02 (20060101); C12P 7/64 (20060101); A01H

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date FEB -9 1998

From Acting Director, Division of Programs and Enforcement Policy, Office of Special Nutritionals, HFS-455

2587 '98 MAR 17 P1:4

Subject 75-Day Premarket Notification for New Dietary Ingredients

To Dockets Management Branch, HFS-305

New Dietary Ingredient:	SeaGold™DHA-rich oil
Firm:	Monsanto Company
Date Received by FDA:	December 22, 1997
90-Day Date:	March 22, 1998

In accordance with the requirements of section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act, the attached 75-day premarket notification for the aforementioned new dietary ingredient should be placed on public display in docket number 95S-0316 after March 22, 1998.

Sincerely yours,

for James Tanner, Ph.D.
Acting Director,
Division of Programs and
Enforcement Policy
Office of Special Nutritionals
Center for Food Safety and
Applied Nutrition

Attachment

cc:
HFS-22, CCO
HFS-450 (r/f, OSN w/control slip:TRAC#56528 & cpy incoming)
HFS-456 (r/f, Latham, Moore)
r/d:HFS-456:JELatham:jel:01/30/98:DocName:#56528.mem:Disc4

95S-0316

RPT 17

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Washington, DC 20204

FEB -9 1998

Dr. Wayne Stargel, Pharm.D.
Vice President, Regulatory Affairs
Monsanto Company
5200 Old Orchard Road
Skokie, Illinois 60077

Dear Dr. Stargel:

This is to notify you that your submission pursuant to section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the act) dated December 19, 1997, concerning the marketing of a substance that you assert is a new dietary ingredient (i.e., SeaGold™DHA-rich oil) was received by the Food and Drug Administration (FDA) on December 22, 1997. Your submission will be kept confidential for 90 days from the date of receipt, and after March 22, 1998, your submission will be placed on public display at Dockets Management Branch (Docket No. 95S-0316). Commercial and confidential information in the notification will not be made available to the public.

Please contact us if you have questions concerning this matter.

Sincerely yours,

James Tanner, Ph.D.
Acting Director
Division of Programs and
Enforcement Policy
Office of Special Nutritionals
Center for Food Safety
and Applied Nutrition

Monsanto

Monsanto Company
5200 Old Orchard Road
Skokie, IL 60077
Phone: (847) 982-7000

December 19, 1997

Notification of New Dietary Ingredient

Office of Special Nutritionals (HFS-450)
Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration
200 C Street, SW
Washington, DC 20204

To the Food and Drug Administration (FDA):

Pursuant to the Dietary Supplement Health and Education Act of 1994 (DSHEA), 21 U.S.C. § 350b (a) (2), and consistent with the new final regulations published by the FDA in the Federal Register of September 23, 1997 (62 Fed. Reg. 49886-49892), 21 C.F.R. § 190.6, "Requirement for premarket notification," Monsanto hereby submits the following information concerning a new dietary ingredient that Monsanto intends to begin marketing for use in dietary supplements. The new ingredient contains, with the possible exception of one component present in small amounts, only components already present in the food supply. Pursuant to the applicable provisions of the DSHEA, 21 U.S.C. § 350b (a) (2), Monsanto will not introduce the ingredient or deliver it for introduction into interstate commerce until at least 75 days after the date on which FDA receives this notification.

(1) NAME AND ADDRESS OF MANUFACTURER

The name and complete address of the manufacturer of the new dietary ingredient are as follows:

Manufacturer:
Monsanto Company
800 N. Lindbergh Blvd.
St. Louis, MO 63167

Direct correspondence to:
Robert C. Peterson
Monsanto Company
Worldwide Regulatory Affairs
5200 Old Orchard Road
Skokie, IL 60077

(2) NAME OF NEW DIETARY INGREDIENT

The name of the new dietary ingredient is as follows:

SeaGold™ DHA-rich oil. DHA refers to 4,7,10,13,16,19-docosahexaenoic acid.

(3) DESCRIPTION

The description of the new dietary ingredient is as follows:

SeaGold™ DHA-rich oil is a yellow to light orange-colored oil derived from the heterotrophically grown marine microalgae, *Schizochytrium* sp. The oil is refined, bleached, deodorized, and contains natural tocopherols, ascorbyl palmitate and lecithin or other safe and suitable components for stabilization. d,l-α-tocopheryl acetate may also be added to increase the intake of Vitamin E.

Labeling for the new dietary ingredient will specify that it should be used at up to 1 gram of DHA-rich oil per day to increase the intake DHA.

(4) BASIS FOR THE SAFETY OF DHA-RICH OIL

Summary

SeaGold™, a DHA rich oil, is a new dietary ingredient for use in dietary supplements, derived from the heterotrophically grown marine microalgae, *Schizochytrium* sp. DHA is the most abundant polyunsaturated fatty acid (PUFA) component of the oil (approx. 35% w/w). The oil is intended for use as an ingredient in dietary supplements to increase DHA intake. The suggested intake is up to 1 gram of oil containing up to 350 mg DHA per day. Research has indicated it may be desirable to increase n-3 PUFA intake. Current estimated intake of long chain (LC) n-3 PUFA (eicosapentaenoic acid (EPA) plus DHA) is 75-100 mg/d (Raper *et al*, 1992; Douglass *et al*, 1995). Recommended intakes as high as 800 mg of EPA plus DHA per day have been made (British Nutrition Foundation, 1992).

The microalgal oil source, *Schizochytrium* sp., is a thraustochytrid, a member of the kingdom Chromista. *Schizochytrium* sp. occurs widely in the marine environment and is an indirect component of the human food chain through consumption of fish and other marine animals that feed on the *Schizochytrium* sp. microalgae. There have never been any reports of toxic compounds being produced by members of the thraustochytrids.

The safety of DHA-rich oil is based on the inherent safety of the fatty acid and sterol components of the oil. The safety of these components is based on their history of safe use in food, the small quantities expected to be consumed, extensive knowledge of their metabolism, published safety studies, and the absence of reports of toxicity. The safety is further supported by published studies on a microalgal oil nutritional supplement of similar composition, by the historical safe use of fish oil nutritional supplements of similar

composition, and by corroborative safety studies of the dried microalgal source of the DHA-rich oil.

Manufacture of DHA-rich oil

DHA-rich oil is extracted from dried microalgae which are produced from a fermentation process using a microalgae from the genus *Schizochytrium* sp. The algae are grown via a pure culture heterotrophic fed-batch fermentation process. The organism used is an improved strain of the original wild-type culture (*Schizochytrium* sp. ATCC 20888). The improved strain was derived using a classical mutagenesis screening program, which employed well-accepted techniques commonly used in industrial microbiologic strain improvement programs. The dried microalgae intermediate product is wet milled using commercial-grade n-hexane via a two-stage counter-current process. The solvent is partially removed from the miscella (mixture of oil and solvent), after which the oil concentration is adjusted to ~45 wt% by adding fresh commercial-grade n-hexane. The miscella is chilled to approximately -1°C and held for at least five hours. After filtering and removal of solvent the oil is refined, bleached and deodorized using standard food industry procedures. The National Research Council (1989) suggested that diets contain approximately 0.4 mg d-α-tocopherol per g of PUFA. Therefore, 3 mg of d,l-α-tocopherol acetate are added per g of DHA-rich oil during processing, an amount that amply satisfies this recommendation.

Composition of DHA-rich oil

The fatty acid composition of the DHA-rich oil was determined by a validated method and is shown in Table 1. The DHA-rich oil contained 3.1 ± 1.0% (average ± std. dev., n=5) unsaponifiable material. The sterols present in the unsaponifiable fraction were qualitatively analyzed by gas chromatography-mass spectrometry. Their approximate proportions were determined by peak area % (see Table 2).

Martek®
Martek Biosciences Corporation

August 18, 2003

BY HAND DELIVERY

Mr. Richard E. Bonnette
Consumer Safety Officer
Office of Premarket Approval (HFS-255)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
200 C Street SW
Washington, D.C. 20204

Re: GRAS Exemption Claim for DHA Algal Oil Derived from *Schizochytrium* sp. as a Source of DHA for Use in Foods

Dear Mr. Bonnette:

Pursuant to proposed 21 CFR 170.36, 62 Fed. Reg. 18938 (April 17, 1997), Martek Biosciences Corporation hereby provides notice of a claim that docosahexaenoic acid (DHA) oil from *Schizochytrium* sp. (DHA Algal Oil) is exempt from the premarket approval requirement of the Federal Food, Drug, and Cosmetic Act (FFDCA). The summary data and information in this notification establish that DHA Algal Oil is generally recognized as safe (GRAS), based on scientific procedures, for use as a food ingredient to increase dietary intake of DHA up to 1.5 grams of DHA per day.

In accordance with the criteria set forth in the GRAS notification proposed regulation found at 62 Fed. Reg. 18938, 18961 (1997), Martek submits the following information as part of its GRAS exemption claim.

Name and Address of Notifier: Martek Biosciences Corporation, 6480 Dobbin Road, Columbia, Maryland 21045.

Common or Usual Name of the Substances: DHA Algal Oil. This product will be marketed under the tradename, DHASCO®-S.

000004

6480 Dobbin Road
Columbia, Maryland 21045

(410) 740-0081
Fax (410) 740-2985
www.martekbio.com

Applicable Conditions of Use: Use as an ingredient in the food categories for menhaden oil (21 CFR 184.1472(a)(3)) at a level that is approximately 29 percent of the levels listed in that regulation. The DHA Algal Oil is intended for use in those additional food categories covered by the GRAS notification submitted for fish oil concentrate at a level that is 50 percent of the levels covered in GRN 000105.

Basis for GRAS Determination: DHA Algal Oil is GRAS on the basis of scientific procedures.

Availability of Data: The data and information that are the basis for the notifier's GRAS determination are available for the Food and Drug Administration's (FDA) review and copying at reasonable times at the law offices of Hogan & Hartson, L.L.P., 555 13th Street N.W., Washington DC 20004, or will be sent to FDA upon request.

GRAS Exemption Claim: The use of DHA Algal Oil as a food ingredient to increase dietary intake of DHA up to 1.5 grams of DHA per day is exempt from the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act (FFDCA) because Martek, after consulting with a panel of outside experts, has determined that such use is GRAS.

* * * * *

We enclose an original and two copies of this notification for your review. If you have any questions, please contact me at the above phone number and address.

Sincerely,

Sam Zeller, Ph.D.

Enclosures

2. Oil Components

The identified components present in DHA Algal Oil have a demonstrated history of safe consumption. The lipid fraction of *Schizochytrium* sp. algae is comprised mainly of fatty acids and sterols. Fatty acids (Table 3) are found esterified to glycerol (tri- and diacylglycerides) and sterols (steryl esters) and may be present as free fatty acids. Sterols (Table 4) are found as steryl esters and free sterols. Beta-carotene was identified as the primary carotenoid component of the lipid fraction (Zeller et al., 2001).

All fatty acids present in DHA Algal Oil are components of a normal diet or normal metabolites of fatty acids. Recommended use levels will only increase the consumption of two component fatty acids, DHA and docosapentaenoic acid (DPA(n-6)), above that currently consumed from the diet. A comprehensive discussion on the safety of the fatty acid components present in DHA Algal Oil derived from *Schizochytrium* sp. algae along with knowledge of the absorption, distribution, metabolism and excretion of the fatty acids and published safety information on these and similar compounds have previously been provided to the agency as part of a New Dietary Ingredient Premarket Notification filed in December 1997 by Monsanto for SeaGold™ DHA-rich oil—which is the same oil that is the subject of this GRAS notification. [3]/

The non-saponifiable fraction of the DHA Algal Oil consists primarily of squalene, sterols, and carotenoids. These components are all present in the food supply. At the proposed use level for a food ingredient, the estimated consumption of sterols approximates the current consumption of sterols in the general population from other food sources and is likely smaller than some groups within the population such as vegetarians.

Additional information on the safety of the sterol components present in the oil component of *Schizochytrium* sp. algae along with knowledge of the absorption, distribution, metabolism and excretion of sterols and published safety information on these and similar phytosterols has previously been supplied to the agency in the New Dietary Ingredient Premarket Notification submitted by Monsanto in December 1997 for SeaGold™ DHA-rich oil—the same oil that is the subject of this notification. [4]/

3. DHA and DPA(n-6)

Proposed uses of DHA Algal Oil derived from *Schizochytrium* sp. algae as a food ingredient will only increase the consumption of two component fatty acids, DHA and DPA(n-6), above that currently consumed from the diet. FDA has affirmed that the mean consumption of up to 3 g of DHA and EPA (from menhaden oil) per day is GRAS; therefore the proposed consumption of up to 1.5 g DHA per day from DHA Algal Oil is considered safe.

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[3]/ See http://www.fda.gov/ohrms/dockets/dockets/95s0316/rpt0017_01.pdf

[4]/ See http://www.fda.gov/ohrms/dockets/dockets/95s0316/rpt0017_01.pdf.

Policy Memorandum

To: Stakeholders and interested parties

From: Miles McEvoy, Deputy Administrator

Subject: Clarification of Existing Regulations Regarding the Use of Genetically Modified Organisms in Organic Production and Handling

Date: April 15, 2011

The National Organic Program (NOP) has recently received questions concerning the use of genetically modified organisms (GMOs) under the U.S. National Organic Standards. This policy memorandum addresses frequently asked questions concerning GMOs and reiterates the statements made in a 2004 letter from USDA Undersecretary Bill Hawks to the National Association of State Departments of Agriculture.

Compliance with the organic standards entails that operations have verifiable practices in place to avoid contact with GMOs. Since organic certification is process-based, presence of detectable GMO residues alone does not necessarily constitute a violation of the regulation. The NOP relies on organic certifiers and producers to determine preventative practices that most effectively avoid contact with GMOs on an organic operation.

The use of GMOs is prohibited in organic production and handling. The NOP regulations prohibit the use of GMOs as "excluded methods" under 7 CFR § 205.105, "Allowed and prohibited substances, methods, and ingredients in organic production and handling." Excluded methods are defined as:

> A variety of methods to genetically modify organisms or influence their growth and development by means that are not possible under natural conditions or processes and are not considered compatible with organic production. Such methods include cell fusion, microencapsulation and macroencapsulation, and recombinant DNA technology (including gene deletion, gene doubling, introducing a foreign gene, and changing the positions of genes when achieved by recombinant DNA technology). Such methods do not include the use of traditional breeding, conjugation, fermentation, hybridization, in vitro fertilization, or tissue culture. (7 CFR § 205.2-Terms defined)

This policy memo reiterates that the use of GMOs is prohibited under the NOP regulations and answers questions that have been raised concerning GMOs and organic production and handling.

Issue: If a producer adheres to all aspects of the NOP regulations, including never utilizing genetically modified seeds, but a certifying agent tests and detects the presence of genetically modified material in the crop, is that crop's status determined to be no longer certified organic?

Reply: Organic certification is process based. That is, certifying agents attest to the ability of organic operations to follow a set of production standards and practices which meet the requirements of the Organic Foods Production Act of 1990 and the NOP regulations. The NOP regulations prohibit the use of excluded methods (i.e., "GMOs") in organic operations. If all aspects of the organic production or handling process were followed correctly, then the presence of a detectable residue from a genetically modified organism alone does not constitute a violation of this regulation. This policy was established at the promulgation of the NOP Regulation in the Preamble to the Final Rule (FR Vol. 65, No. 246, p. 80556), December 21, 2000. The Preamble stated that:

> As long as an organic operation has not used excluded methods and takes reasonable steps to avoid contact with the products of excluded methods as detailed in their approved organic system plan, the unintentional presence of the products of excluded methods should not affect the status of the organic operation or its organic products.

Issue: Is the inadvertent presence of GMOs in organic seeds a violation of the NOP regulations? Can organic producers use seeds that contain the inadvertent presence of GMOs?

Reply: 7 CFR § 205.105 of the NOP regulations prohibits the use of GMOs as excluded methods in organic production and handling. The use of excluded methods, such as planting genetically modified seeds, would require a specific intent, and would render any product ineligible for organic certification. However, the inadvertent presence of GMOs in organic seeds does not constitute a use because there was no intent on the part of the certified operation to use excluded methods. The presence of detectable GMO residues alone in an organic seed does not constitute a violation of the NOP regulations.

Issue: How do organic producers avoid contact with GMOs?

Reply: Organic producers utilize a variety of methods to avoid contact or the unintentional presence of GMOs including testing seed sources for GMO presence, delayed or early planting to get different flowering times for organic and GMO crops, cooperative agreements with neighbors to avoid planting GMO crops adjacent to organic crops, cutting or mowing alfalfa prior to flowering, posting signs to notify neighboring farmers of the location of organic fields, and thorough cleaning of farm equipment that has been used in non-organic crop production.

Issue: What are organic producers required to do in order to avoid the presence of GMOs in their products?

Reply: In order to become a certified organic operation, a producer must submit an organic system plan to a NOP accredited certifying agent for approval. The producer's organic system

plan must include a description of management practices and physical barriers established to prevent contact of organic crops with prohibited substances. Certifying agents evaluate the preventative practices and buffer zones to determine if the producer has taken reasonable steps to avoid contact with GMOs.

Issue: Could a farm's organic certification status be threatened if sufficient buffers and barriers are not established and inadvertent contact with GMO material occurs?

Reply: Organic producers that implement preventive measures to avoid contact with GMOs will not have their certification threatened from the inadvertent presence of the products of excluded methods (GMOs). Crops grown on certified organic operation may be sold, labeled and represented as organic, even with the inadvertent presence of GMOs, provided that all organic requirements under 7 CFR Part 205 have been followed.

Issue: Is there a working definition of the word "contamination" within the NOP?

Reply: There is no definition in the NOP regulations for the word "contamination," even though it is mentioned frequently in the standards. The use of excluded methods in organic production is prohibited, as cited in 7 CFR § 205.105.

Issue: What actions are authorized or required when organic crops or products are found to contain unintended or inadvertent genetically modified substances?

Reply: The inadvertent presence of genetically modified material does not affect the status of the certified operation and does not result in loss of organic status for the organic product, provided it was produced in accordance with all of the organic requirements under 7 CFR Part 205. Certifying agents are responsible for working with organic producers to identify the source of the inadvertent GMOs and to implement reasonable steps to avoid contact with GMOs in the future.

Issue: Are organic products tested for genetically modified substances?

Reply: Under 7 CFR § 205.670(b) certifying agents may test organic products when there is reason to believe that excluded methods were used in the production or handling of an organic agricultural product. Certifying agents may also collect and test organic products from organic handlers to ensure that practices are in place to prevent commingling or contamination during handling and processing.

Issue: Are organic products free of GMO contaminants?

Reply: Organic standards are process based. The NOP regulations prohibit the use of genetically modified organisms, prohibit commingling or contamination during processing and handling, and require preventative practices to avoid contact with GMOs. Organic agricultural products should have minimal if any GMO contaminants; however, organic food products do not have a zero tolerance for the presence of GMO material.

Issue: Has a tolerance level (e.g. 5%) been established for the presence of GMOs in organic agricultural products?

Reply: The NOP regulations do not establish GMO tolerance levels. The NOP regulations establish a tolerance for the presence of pesticides registered by the U.S. Environmental Protection Agency (EPA) that is set at 5% of the EPA tolerance level for the specific residue detected. No federal agency, including EPA or USDA has established tolerance levels for the inadvertent presence of the products of excluded methods (GMOs).

Issue: Processed foods sold as "organic" must contain at least 95% organic ingredients. Are GMOs allowed in the remaining 5% of ingredients? Likewise, processed foods sold as "made with organic (specified ingredients or food group(s))" must contain at least 70% organic ingredients. Are GMOs allowed in the remaining 30% of ingredients for these products?

Reply: The use of GMOs is prohibited in all ingredients in "organic" and "made with organic (specified ingredients or food groups(s))." There is no provision within the NOP regulations that allows the use of excluded methods (GMOs) in ingredients or processing aids under the "organic" or "made with organic (specified ingredients or food group(s))" label categories.