Docosahexaeenzuurrijke olie

Tweede beoordeling van de veiligheid voor de consument, volgens de Europese verordening 258/97 betreffende nieuwe voedingsmiddelen en nieuwe voedselingrediënten

Docosahexaenoic acid rich oil

Second opinion regarding consumer safety, in accordance with European Regulation 258/97 concerning novel foods and novel food ingredients

Gezondheidsraad:
Commissie Veiligheidsbeoordeling nieuwe voedingsmiddelen (VNV)

Health Council of the Netherlands:
Committee on the Safety Assessment of Novel Foods

aan/to:

de Minister van Volksgezondheid, Welzijn en Sport/
the Minister of Health, Welfare and Sport

de Minister van Landbouw, Natuurbeheer en Visserij/
the Minister of Agriculture, Nature management and Fisheries

Nr. 2002/03VNV, Den Haag, 26 augustus 2002
No. 2002/03VNV, The Hague, August 26 , 2002

De Gezondheidsraad, ingesteld in 1902, is een adviesorgaan met als taak de regering en het parlement “voor te lichten over de stand der wetenschap ten aanzien van vraagstukken op het gebied van de volksgezondheid”(art. 21 Gezondheidswet).

De Gezondheidsraad ontvangt de meeste adviesaanvragen van de bewindslieden van Volksgezondheid, Welzijn & Sport; Volkshuisvesting, Ruimtelijke Ordening & Milieubeheer; Sociale Zaken & Werkgelegenheid en Landbouw, Natuurbeheer & Visserij. De Raad kan ook eigener beweging adviezen uitbrengen. Het gaat dan als regel om het signaleren van ontwikkelingen of trends die van belang kunnen zijn voor het overheidsbeleid.

De adviezen van de Gezondheidsraad zijn openbaar en worden in bijna alle gevallen opgesteld door multidisciplinair samengestelde commissies van -op persoonlijke titel benoemde- Nederlandse en soms buitenlandse deskundigen.

The Health Council of the Netherlands, established in 1902, is an independent scientific advisory body. Its remit is “to advise the government and Parliament on the current level of knowledge with respect tot public health issues” (Section 21, Health Act).

The Health Council receives most requests for advice from the Ministers of Health, Welfare & Sport; Housing, Spatial Planning & the Environment; Social Affairs & Employment, and Agriculture, Nature management & Fisheries.

Most Health Council reports are prepared by multidisciplinary committees of Dutch or, sometimes, foreign experts, appointed in a personal capacity. The reports are available to the public.

Deze publicatie kan als volgt worden aangehaald:
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Inhoud/Contents

Aanbiedingsbrief (4 A4tjes)

Letter to the Dutch Minister of Health, Welfare and Sport

On August 26, 2002, professor JGAJ Hautvast, Vice-president of the Health Council of the Netherlands wrote as follows to the Minister of Health, Welfare and Sport:

This letter has been prepared in reply to your request for advice regarding the safety of novel foods and food ingredients, also made on behalf of the Minister of Agriculture, Nature Management and Fisheries. The subject in question is a so-called second opinion, in accordance with European Regulation 258/97, concerning a docosahexaenoic-acid-rich oil. The applicant, the company OmegaTech, is going to market this oil under the trade name of DHA Gold™ (DHA: docosahexaenoic acid). The oil is being produced using the microalgae *Schizochytrium* sp. The new product will not be directly available for consumers, but will be incorporated in variety of foodstuffs. This assessment has been carried out by the 'Committee on Safety Assessment of Novel Foods' (VNV Committee) of the Health Council of the Netherlands.

The initial assessment of the application for market introduction was carried out in the United Kingdom by the Advisory Committee on Novel Foods and Processes (ACNFP) of the Food Standards Agency. The ACNFP concluded that the DHA-rich oil is safe for consumption as a food ingredient to be used as indicated in the dossier. The Committee based its view on scientific knowledge of fatty-acid metabolism, current human dietary exposure levels and safety studies carried out by the applicant. The ACNFP states that the applicant, who manufactures the oil, has agreed to inform those food producers wishing to incorporate the oil into their products of the recommended

daily dietary allowance of DHA. This information must be made available to consumers by means of appropriate labelling of the DHA-enriched final food products.

The VNV Committee based its views on the report of the initial assessment by the ACNFP and on the information contained in the dossier. The VNV Committee largely agrees with the British assessment. It appears that, in terms of quality, the production process incorporates the necessary safeguards. The DHA content of the oil is 35 to 45%, and it contains neither undesirable components nor microbiological contaminants.

From the nutritional point of view, there is no objection to the use of this oil whose identified ingredients are already present in our normal diet to some degree. With a view to the potential health benefits, various national and international scientific organisations and advisory councils recommend a daily intake of the so-called fish-oil fatty acids, eicosapentaenoic acid (EPA) and DHA. This recommended intake varies considerably, not just at the global level, but also within Europe itself. The values range from 200 mg to almost 2000 mg per individual per day. The VNV Committee notes that, in the Netherlands, a relatively low intake of fish-oil fatty acids is recommended. Last year, the Health Council has published an advisory report entitled 'Dietary reference intakes: energy, proteins, fats, and digestible carbohydrates' (GR01). This report put forward the view that an average daily intake of 200 mg of fish-oil fatty acids is sufficient to produce beneficial health effects, namely reduced mortality from cardiovascular diseases. It was not possible to draw up separate standards for EPA and DHA.

On average, UK adults currently consume 107 mg of DHA per day as part of their normal diet. As a supplement to the initial assessment, the VNV Committee concludes that the DHA intake data for inhabitants of the other EC member states is too poorly supported. This is because these are based on the FAO Food Balance Sheets, which only indicate how much of a given foodstuff is available per head of population. The Committee therefore wonders to what extent UK consumers, about whom the dossier does provide detailed and reliable food-consumption information, are representative of the European population as a whole.

The applicant proposes 550 mg per day as the intended total DHA intake value. The amount of DHA in the normal diet could thus be supplemented with about 440 mg of DHA from the new oil. To this end, one or two portions of a product that has been enriched with DHA Gold oil should be sufficient. However, this level of intake is close to the upper DHA intake level that is considered to be safe by the United States FDA (1997), namely 1500 mg per day. Based on the results of extensive toxicological studies in experimental animals and safety studies in humans, the ACNFP concludes that there is no evidence that such high levels of consumption would lead to adverse

health effects. The VNV Committee concurs with this view. On safety grounds, it has therefore no objections to the new product being placed on the market for the intended purpose of achieving an additional daily intake of about 440 mg of DHA. However, the VNV Committee does foresee practical problems given the margin of a factor of three between the intented intake and the safe upper level of intake. A major point of criticism is that the applicant has failed to provide specific details of the range of foodstuffs into which the DHA-rich oil would be incorporated. Also, the Committee is not convinced that consumers would limit themselves to just one of the DHA-enriched products per day, as suggested by the applicant. In addition, the VNV Committee would like to point out that Dutch supermarkets already stock products with elevated DHA levels.

The applicant company OmegaTech, which produces the new oil, has agreed to advise end-producers of the DHA-enriched foodstuffs concerning appropriate use of DHA Gold. However, the VNV Committee feels that this promise is too vaguely worded. The VNV Committee very much doubts that this would prevent the safe upper intake level from being exceeded. It is by no means clear how the applicant can be expected to monitor all possible uses of the new ingredient. The VNV Committee proposes that the new oil should only be approved for use in a limited and well defined range of products. It agrees with the ACNFP, which has imposed additional labelling requirements to ensure that consumers are informed both about the recommended dietary allowance of DHA and the safe upper intake level. The Commission would also like to highlight the option of post marketing surveillance, to determine the extent to which the intake guarantees can be met.

The VNV Committee has established that there is a need for improved scientific support for the maximum safe level of intake of fish-oil fatty acid, providing a better understanding of possible long-term effects. It has been found that exceeding the upper intake level has an effect on blood coagulation. Given the current level of scientific knowledge, it is not known to what extent this might result in adverse health effects. Finally, the VNV Committee points out that additional toxicological information is required in case the DHA-rich oil will be used in infant formulae. The toxicological data provided in the dossier is insufficient for an evaluation of the safety of this specific application.

In summary, the VNV Committee does not object to authorisation of the new ingredient DHA GoldTM on the European market, provided that it is incorporated into a limited and well-defined range of foodstuffs. Each product must be clearly labelled, indicating the recommended daily dietary allowance for fish-oil fatty acids, the group of substances to which DHA belongs. As a precautionary measure, the Committee recommends that also a maximum daily number of servings should be indicated on the

label, because it is not known for certain whether adverse health effects can be excluded by exceeding an intake of 1500 mg.

I endorse the conclusions and recommendations of the VNV Committee,

(signed) professor JGAJ Hautvast

Literatuur/Literature

EC97 Verordening (EC) Nr. 258/97 van het Europees Parlement en de Raad van 27 januari 1997 betreffende nieuwe voedingsmiddelen en nieuwe voedselingrediënten. Publikatieblad van de Europese Gemeenschappen 1997; L43: 1-6 (Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients. Official Journal 1997; L 043: 1-6)

EC97a 97/618/EC: Aanbeveling van de Commissie van 29 juli 1997 betreffende de wetenschappelijke aspecten en de presentatie van de informatie die nodig is om aanvragen voor het in de handel brengen van nieuwe voedingsmiddelen en nieuwe voedselingrediënten te ondersteunen alsmede het opstellen van de verslagen van de eerste beoordeling uit hoofde van Verordening (EC) nr. 258/97 van het Europees Parlement en de Raad. Publicatieblad van de Europese Gemeenschappen 1997; L253: 1-36 (97/618/EC: Commission Recommendation of 29 July 1997 concerning the scientific aspects and the presentation of information necessary to support applications for the placing on the market of novel foods and novel food ingredients and the preparation of initial assessment reports under Regulation (EC) No 258/97 of the European Parliament of the Council. Official Journal 1997; L 253: 1-36)

FAO96 Biotechnology and Food Safety. Report of a joint FAO/WHO Consultation. Rome, FAO 1996.

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GR92 Commissie Toxicologische aspecten van biotechnologisch bereide producten. Productveiligheid bij nieuwe biotechnologie. Den Haag, Gezondheidsraad 1992, publicatienummer 1992/03.

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OECD00 Report of the task force for the safety of novel foods and feeds. Paris, OECD 2000.

SCF99 Opinion concerning the scientific basis for determining whether food products, derived from genetically modified maize, could be included in a list of food products which do not require labelling because they do not contain (detectable) traces of DNA or protein. Brussels, Scientific Committee on Food of the EU 1999.

SSC99 Opinion of the Scientific Steering Committee on microbial resistance, Brussels, Scientific Steering Committee of the EU 1999.

WHO91 Strategies for assessing the safety of foods produced by biotechnology. Report of a joint FAO/WHO Consultation. Geneva, WHO 1991.

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A	De adviesaanvraag/Request for advice
B	De commissie/The committee
C	EU-procedure/EU-procedure
D	Samenvatting van het dossier/Executive summary of the dossier
E	Eerste beoordeling/First assessment

Bijlagen/Annexes

Bijlage **A**

De Adviesaanvraag/Request for advice

Op 18 augustus 1999 schreef de Minister van Volksgezondheid, Welzijn en Sport aan de Voorzitter van de Gezondheidsraad (brief kenmerk GZB/VVB 993428):

Sinds mei 1997 is in de Europese Unie de Verordening (EG) 258/97 van kracht inzake nieuwe voedingsmiddelen en nieuwe voedselingrediënten. Daarmee werd de veiligheidsbeoordeling onderdeel van een communautaire procedure.

Met u is reeds de mogelijkheid besproken de beoordeling door de Gezondheidsraad te laten uitvoeren. Ik verzoek u dan ook mede namens de Staatssecretaris van Landbouw, Natuurbeheer en Visserij, in deze eerste fase van uitvoering van de Europese Verordening (EG) 258/97 gedurende een aantal jaren, de veiligheidsbeoordeling gestalte te geven. Voor het onderbrengen bij de Gezondheidsraad pleit het experimentele karakter dat de beoordeling de eerste jaren zal hebben. Dit experimentele karakter komt voort uit het feit dat het een nieuw soort beoordeling betreft van deels nieuwe categorieën van voedingsmiddelen of voedselingrediënten. Het is namelijk een veiligheidsbeoordeling vóór het op de markt brengen van met name voedingsmiddelen van een genetisch gemodificeerde oorsprong en zogenaamd functional foods (nutriceutica). Daarnaast ga ik ervan uit dat de onafhankelijke wetenschappelijke advisering door de Gezondheidsraad het vertrouwen van de Europese Commissie en de andere lidstaten in het Nederlandse oordeel nog versterkt.

Mijn beleid is erop gericht een zo groot mogelijke openheid en transparantie te realiseren van de gevolgde procedure en de beoordeling om de consument vertrouwen te geven in de veiligheid van de nieuwe

voedingsmiddelen. Ik verzoek de Gezondheidsraad hieraan bij te dragen door bijvoorbeeld inzage te geven in de dossiers waarvoor een aanvraag wordt ingediend, waarbij uiteraard bedrijfsvertrouwelijke gegevens worden beschermd en door de criteria, waarop de veiligheid zal worden beoordeeld, te publiceren.

De Minister van Volksgezondheid, Welzijn en Sport,
w.g. dr E Borst-Eilers

English translation

On 18 August 1999, the Minister of Health, Welfare and Sport wrote as follows to the President of the Health Council of the Netherlands (under reference GZB/VVB 993428):

Since May 1997, Regulation (EC) 258/97 concerning novel foods and novel food ingredients has been in force in the European Union. Under the Regulation, the safety of novel foods has to be assessed as part of a community procedure.

Following discussions regarding the possibility of the Health Council making such assessments, the State Secretary for Agriculture, Nature Management and Fisheries and I wish the Council to take responsibility for safety assessment for a period of several years during the fist phase of implementation of European Regulation (EC) 258/97. It is considered appropriate that the Health Council should initially take on this role because the assessment activities will be of an experimental nature, involving both a new form of assessment (i.e. pre-marketing assessment) and, in many cases, new categories of foodstuff (primarily foodstuffs with a genetically modified basis and functional foods or nutraceuticals). We also feel that if assessments are made by a body with the Council's independent scientific status, this will support the validity of the Netherlands' opinion in the eyes of the European Committee and other member states.

My wish is to make the procedure and the assessment as open and transparent as possible, so as to enhance consumer trust in the safety of novel foods. I would like the Health Council to support this objective by, for example, allowing perusal of the application dossier (insofar as consistent with the need to protect the confidentiality of commercially sensitive information) and publishing the criteria upon which safety assessments are made.

The Minister of Health, Welfare and Sport,
(signed) dr E Borst-Eilers

Bijlage **B**

De commissie/The committee

- Prof. dr LM Schoonhoven, *voorzitter/chairman*
  emeritus hoogleraar entomologie; Wageningen Universiteit en Researchcentrum/
  emeritus professor of entomology; Wageningen University and Research centre
- Prof. dr CAFM Bruijnzeel-Koomen
  hoogleraar dermatologie/allergologie; Academisch Ziekenhuis Utrecht/
  professor of dermatology/allergology; Academic Hospital Utrecht
- Ir EJ Kok
  toxicoloog; RIKILT-DLO Wageningen/toxicologist; State Institute for Quality Control of Agricultural Products, Wageningen
- Dr CF van Kreijl
  moleculair-bioloog; RIVM Bilthoven/molecular biologist; National Institute of Public Health and the Environment, Bilthoven
- Prof. dr P van der Laan
  hoogleraar statistiek; Technische Universiteit Eindhoven/
  professor of statistics; Technical University Eindhoven
- Dr B Loos, *adviseur/advisor*
  COGEM, Den Haag/Committee on Genetic Modification, The Hague
- Dr F Nagengast
  gastro-enteroloog; Academisch Ziekenhuis Nijmegen/
  gastro-enterologist; Academic Hospital Nijmegen

- Dr JMA van Raaij
  voedingsfysioloog; Wageningen Universiteit and Researchcentrum/
  food physiologist; Wageningen University and Research centre
- Prof. dr G Schaafsma
  hoogleraar voeding; TNO Voeding, Zeist/
  professor of nutrition; TNO Nutrition and Food Research, Zeist
- Prof. dr EG Schouten
  hoogleraar epidemiologie; Wageningen Universiteit and Researchcentrum/
  professor of epidemiology; Wageningen University and Research centre
- Dr GJA Speijers
  toxicoloog; RIVM Bilthoven/toxicologist; National Institute of Public Health and the Environment, Bilthoven
- Prof. dr WJ Stiekema
  hoogleraar bioinformatica; Wageningen Universiteit en Researchcentrum/
  professor of bioinformatics; Wageningen University and Research centre
- Ir R Top, *adviseur/advisor*
  Ministerie van VWS; Den Haag/
  Ministry of Health, Welfare and Sport; The Hague
- Prof. dr WM de Vos
  hoogleraar microbiologie; Wageningen Universiteit en Researchcentrum/ professor of microbiology; Wageningen University and Research centre
- Dr RA Woutersen
  toxicoloog; TNO Voeding, Zeist/
  toxicologist; TNO Nutrition and Food Research, Zeist
- Dr ir M Rutgers, *secretaris/scientific staff member*
  Gezondheidsraad, Den Haag/Health Council of the Netherlands, The Hague

Administratieve ondersteuning/Administrative assistance: AD Lugtenburg
Gezondheidsraad, Den Haag/Health Council of the Netherlands, The Hague
Lay-out: J van Kan
Gezondheidsraad, Den Haag/Health Council of the Netherlands, The Hague

Bijlage **C**

EU-procedure/EU-procedure

Als een fabrikant een nieuw voedingsmiddel op de markt brengt, dient de veiligheid voor de consument gewaarborgd te zijn. In 1997 werd de Europese verordening van kracht waarin de procedure is geregeld voor de goedkeuring voor marktintroductie van een nieuw voedingsmiddel (EC97). Bij deze procedure zijn verschillende actoren betrokken. De aanvrager moet beoordelen of het product werkelijk ‘nieuw’ is, dat wil zeggen dat het nog niet eerder in de Europese Unie in substantiële mate voor menselijke voeding is gebruikt en ook niet wezenlijk gelijkwaardig is aan een bestaand product. (Voor een wezenlijk gelijkwaardig product kan worden volstaan met een kennisgeving van de marktintroductie.) Ook moet het niet gaan om een levensmiddelenadditief, aroma of extractiemiddel, omdat deze producten op een andere wijze worden beoordeeld. Voor een nieuw voedingsmiddel in de zin van de Europese verordening moet de aanvrager een veiligheidsdossier overleggen volgens aanbevelingen van de Europese Commissie (EC97a). Deze aanbevelingen zijn gebaseerd op rapporten van verschillende instanties die zich met het onderwerp nieuwe voedingsmiddelen bezighouden, te weten de OECD (OECD93, OECD96) en de WHO/FAO (FAO96, WHO91). Ook de Gezondheidsraad heeft zich al eerder over dit onderwerp gebogen (GR92). Sinds het verschijnen van de aanbevelingen van de EU wordt in internationaal verband gewerkt aan explicitering en aanpassing aan de stand van de wetenschap (FAO01, OECD98, OECD00, SCF99, SSC99, WHO00).

De fabrikant levert het volgens de richtlijnen samengestelde dossier in bij het land waar het product het eerst op de markt zal komen. Daarop komt de nationale

veiligheidsbeoordelingsautoriteit in actie. In Nederland is dat de Minister van Volksgezondheid, Welzijn en Sport. Zij heeft de Gezondheidsraad verzocht haar van advies te dienen. De Voorzitter van de Gezondheidsraad heeft hiertoe de commissie Veiligheidsbeoordeling nieuwe voedingsmiddelen (commissie VNV) ingesteld.

De commissie beoordeelt op basis van de huidige stand van de wetenschap of de door de fabrikant geleverde gegevens juist en volledig zijn en of zij het eens is met diens conclusies. Zij maakt een verslag van haar bevindingen — ook volgens de Europese aanbevelingen (EC97a, deel III) — en biedt dat de minister aan. De minister formuleert het Nederlandse oordeel over een voedingsmiddel en brengt dat in bij het Europese overleg in het Permanent Comité voor levensmiddelen. Alle Europese lidstaten worden uitgenodigd hun oordeel (de zogeheten tweede beoordeling) te geven over het dossier en over de eerste beoordeling alvorens genoemd Comité een eindoordeel velt. Als een dossier veel vragen oproept, gaat er een adviesvraag van de Europese Commissie naar het Wetenschappelijk Comité voor de menselijke voeding. Komt men dan nog niet tot overeenstemming dan beslist de Europese Ministerraad.

English translation

When manufacturers bring novel foodstuffs onto the market, consumer safety has to be ensured. In 1997, a European Regulation (EC97) came into force, laying down the procedure for approving the market introduction of novel foodstuffs. The procedure recognizes various actors. The applicant must decide whether a product is a novel foodstuff, i.e. a substance that has not previously been available for human consumption to any substantial extent within the European Union and is not substantially equivalent to any existing product. (If a foodstuff is substantially equivalent to any existing product, it is sufficient to inform the authorities of its market introduction). Food additives, aromas and extracts are excluded from the provisions of the directive, since they fall within the scope of an established assessment regime. Before marketing a novel foodstuff, the applicant must compile a safety dossier that complies with the Recommendations of the European Commission (EC97a). These Recommendations are based on reports by a number of bodies that have studied the issue of novel foodstuffs, in particular the OECD (OECD93, OECD96) and the WHO/FAO (FAO96, WHO91). The Health Council of the Netherlands has also considered the question earlier (GR92). Since publication of the EU recommendations, international efforts have been made to clarify and adapt the latest scientific knowledge in the field (FAO01, OECD98, OECD00, SCF99, SSC99, WHO00).

Having compiled a dossier in line with the guidelines, the manufacturer has to submit it to the competent authority in the country where the product is to be marketed first. This dossier is assessed by the national safety assessment authority. In the

Netherlands, this is the Minister of Health, Welfare and Sport, who is advised by the Health Council. The President of the Health Council has created a Committee on the Safety Assessment of Novel Foods (VNV Committee) to advise the minister on behalf of the Council.

On the basis of the scientific state of the art, the committee has to decide whether the information provided by the manufacturer is accurate and complete and whether the manufacturer's conclusions are sound. The committee then draws up a report on its findings for the minister; this report must also comply with the European Recommendation (EC97a, part III). After considering the report, the minister formulates the Netherlands' opinion regarding the foodstuff in question, which is discussed at European level in the Standing Committee on Foodstuffs. All other European member states are invited to express a 'second opinion' regarding the dossier and the first opinion. The Standing Committee then arrives at a final judgement. If a dossier is particularly contentious, the European Commission calls upon the Scientific Committee on Food for advice. If consensus still cannot be reached, the issue is referred to the European Council of Ministers.

Bijlage **D**

Samenvatting van het dossier/ Executive summary of the dossier

Bijlage **E**

Eerste beoordeling/First assessment