GLOBAL ORGANIZATION FOR EPA AND DHA OMEGA-3S

22 February 2024

To: Mrs. Veerle Vanheusden,

European Commission
DG SANTE - Unit E2 – Food processing technologies and novel foods
Rue Breydel 232
Office B232- 4/45
B-1049 Brussels/Belgium
+32 2 299 06 12
veerle.vanheusden@ec.europa.eu

Dear Mrs. Vanheusden,

This letter has been prepared by GOED, the Global Organization for EPA and DHA Omega-3s. GOED is an international trade association representing the global eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) omega-3 industry. Our 200+ members and partners represent the entire supply chain of EPA and DHA omega-3s, from crude oil producers to refiners, concentrators, contract manufacturers and finished product brands. About 25 percent of our members are European companies, and many other members produce ingredients and finished products that are marketed in the EU. Products produced by our members encompass food supplements (including the ingredient oils for these), DHA-rich oils for use as an ingredient in infant formula, EPA/DHA-rich oils for use as an ingredient in functional foods, and EPA- and EPA/DHA-rich oils for use as active pharmaceutical ingredients (APIs) in pharmaceutical omega-3 products. These products are derived from different fish species from various geographic origins (anchovy oil, cod liver oil, tuna oil, pollock oil, etc.) and omega-3 oils from other marine organisms, as well as microalgal omega-3 oils that originate from microalgae and other microbial species.

GOED writes to provide comments on the proposed SANTE PLAN 2023/2345 Rev.1. and the associated "Discussion paper as regards maximum levels for MOAH in food."

We would like to request the following:

- A delayed implementation for an additional 12 months from the entry into force of the Maximum Limit (ML) for EPA/DHA omega-3 oils from the publication in the Official Journal of the European Union due to the issues identified in this letter. This takes into considerations the need for robust, accurate and selective analytical methods to be developed and made available before Mineral Oil Aromatic Hydrocarbons (MOAH) can be quantified reliably in EPA/DHA omega-3 oils. Only then can a meaningful ML be set and implemented.

  Additionally, while our member companies have been working on this issue for several years, suitable removal technologies remain to be developed in our sector.

- We also request that, given that interlaboratory variability can be as high as 300%, a putative ML of 2 mg/kg for EPA/DHA omega-3 oils allow a tolerance up to 8 mg/kg until the majority of commercial third-party laboratories achieve an interlaboratory variability of max 50%.

- Lastly, and importantly, a ring test for both national reference laboratories and commercial laboratories that companies have access to is needed to determine laboratory proficiencies for MOAH quantification in edible oils, including EPA/DHA-rich oils. Without a ring test and multi-laboratory evaluation that includes omega-3 oils, our members cannot formulate a mitigation plan.

One of the missions of the EC is to ensure the good functioning of the internal market and our suggested approach ensures a balanced and realistic adaptation period for producers, particularly in third countries, to comply with new EU standards, thereby preventing any abrupt disruption in the supply chain while maintaining high standards of food safety.

Below we describe the rationale for our requests.

Key Considerations

The reliable measurement of MOAH in the EPA/DHA omega-3 sector is characterized by several challenges, outlined here.

1. Method uncertainty

GOED is highly concerned about the ability of the current EN 16995 2017 and/or DGF-C-VI 22 (20) method/s to demonstrate compliance with the current EU MOAH action threshold for fats and oils. Even within one laboratory, the variability in results can be marked. Variations up to 300% have been reported, making it very difficult to decide the real value (see examples below).

(*Note: i) The names of third-party laboratories have been anonymized and are reflected by alphabetical letters A, B, C, D, etc., ii) (± x.x value) indicates the measurement uncertainty for a single test result, as provided by the laboratory, and iii) examples are from different GOED member companies.)*

Example 1. The same samples analyzed twice by the same laboratory (B). Values are expressed as MOAH C10-C50 in mg/kg.

Interpretation: Very different results for a replicate analysis.

Product	Test 1	Test 2
A	< 1 (LOQ)	1,1 (± 0,6)
B	< 1 (LOQ)	1,5 (± 0,7)
C	2,0 (± 0,9)	1,6 (± 0,8)

Example 2. The same samples analyzed twice by the same laboratory (B).

Interpretation: About 300% difference in MOAH level for a value close to the harmonized action limit, with large differences in the total MOAH level (C10-50), as well as of individual C-fractions.

Product	Test	MOAH C10-16 mg/kg	MOAH C16-20 mg/kg	MOAH C20-25 mg/kg	MOAH C25-35 mg/kg	MOAH C35-50 mg/kg	MOAH C16-35 mg/kg, sum calc.	MOAH C10-50 mg/kg, sum calc.
A	1	< 0,10	0,17	0,56	3,0	0,68	3,8	**4,5**
	2	< 0,1	< 0,1	0,26	0,6	0,48	0,88	**1,4**

Example 3. Five different batches of the same fish oil product analyzed three times by the same laboratory (A).

Interpretation: The results show a high measurement uncertainty at values close to the current 2,0 mg/kg action limit.

Product	Batch	Test 1 MOAH C10-C50 (mg/kg)	Test 2 MOAH C10-C50 (mg/kg)	Test 3 MOAH C10-C50 (mg/kg)
A	1	2,1 ± 0,9	2,1 ± 0,9	2,1 ± 0,9
	2	2,3 ± 1,0	2,2 ± 0,9	2,1 ± 0,9
	3	2,1 ± 0,9	2,1 ± 0,9	2,1 ± 0,9
	4	2,9 ± 1,2	2,8 ± 1,2	2,9 ± 1,2
	5	3,0 ± 1,2	3,2 ± 1,3	3,2 ± 1,3

When such variations occur at values close to the proposed 2 mg/kg ML, compliance with a potential ML will be at risk for individual companies. Making reliable measurements close to the LOQ is extremely difficult. Also, it makes developing and executing a mitigation plan almost impossible because companies cannot accurately assign a value to a certain MOAH level and decide whether a product meets a putative ML or not. Companies are justifiably hesitant to allocate valuable resources and funding to new mitigation approaches if they cannot reliably measure their outcomes.

Several factors contribute to significant method uncertainty:

i) Firstly, it has been observed by one commercial third-party laboratory that the mCPBA epoxidation reagent used in the sample preparation for MOAH analysis can degrade the internal standards 1- and 2-methylnaphthalene (see Merieux NutriSciences *"Determination of*

Mineral Oil Hydrocarbons in Food and Packaging by Online HPLC-GC-FID and GCxGC-TOF-MS). A correction is made for this by the laboratory, but this is not mentioned in the JRC guidance documents, as far as we know, and it is unknown whether this correction is made by all laboratories. Uncertainty in the amount of internal standard will affect all calculations. Some laboratories have already adopted an alternative epoxidation reagent, performic acid, illustrating that the EN method is being significantly modified and that sample preparation protocols differ between third-party laboratories.

ii) A second challenge is the correct integration of the MOAH "hump" by laboratories. A large variability in procedures is present, as also evident from the recent JRC guidance document. Such apparently small but essential aspects to the already very complicated analysis of this huge analyte group make the accurate quantification of MOAH unreliable.

2. Interlaboratory variability

Besides intra-laboratory variability, an extremely high variability in results is observed between commercial laboratories (ranging up to 300%) for the same sample using the recommended method EN 16995 2017/DGF-C-VI 22 (20) (see examples below). This makes choosing a laboratory to work with very difficult in practice, because nobody knows which laboratory (if any) obtains the correct values.

Example 1. Differences in results and reporting for six samples each analyzed in three different third-party laboratories.

Product	MOAH C10-C50 (mg/kg)		
	Laboratory A	**Laboratory B**	**Laboratory C**
A	< 4 (raised LOQ)	6.7 (± 2.5)	Not reported
B	< 5 (raised LOQ)	4.4 (± 1.7)	Not reported
C	< 5 (raised LOQ)	3.9 (± 1.5)	Not reported
D	10 (± 4)	9.7 (± 1.5)	< 17 (raised LOQ)
E	8.7 (± 3.5)	8.3 (± 3.1)	< 12 (raised LOQ)
F	11 (± 5)	11 (± 4.1)	76

Example 2. The same sample analyzed by three different third-party laboratories.

Product	Laboratory	MOAH C10-16 mg/kg	MOAH C16-20 mg/kg	MOAH C20-25 mg/kg	MOAH C25-35 mg/kg	MOAH C35-50 mg/kg	MOAH C16-35 mg/kg, sum calc.	MOAH C10-50 mg/kg, sum calc.
A	A	< 1	<1		< 3	< 1		**< 3 (raised LOQ)**
	B	< 0,1	< 0,1	1.1	3.8	0.38	4.9	**5.3**
	C							**< 0,5**

Example 3. Five samples analyzed by three different third-party laboratories.

Product	Laboratory A MOAH C10-C50 (mg/kg)	Laboratory B MOAH C10-C50 (mg/kg)	Laboratory D MOAH C10-C50 (mg/kg)
A	<2	-	1,5 ± 0,6
B	<2	-	2,1 ± 0,6
C	<2	-	1,8 ± 0,6
D	<2	-	1,1 ± 0,6
E	<2	2,2 ± 0,93	<2

Example 4. Three omega-3 concentrates analyzed for MOAH content by two different third-party laboratories, with confirmatory analysis for MOAH presence.

Interpretation: While the interlaboratory difference was not extreme for products A and B (*i.e.* the value obtained by laboratory B was within the method uncertainty of laboratory A), there was a marked difference for product C. Despite laboratory B being unable to confirm the presence of MOAH in product C in a qualitative confirmatory analysis, it did not raise the LOQ accordingly. It is impossible to interpret these seemingly contradictory analytical results.

Product	A	B	C
	MOAH C10-C50 (mg/kg)	MOAH C10-C50 (mg/kg)	MOAH C10-C50 (mg/kg)
Laboratory A	5,2 ± 2,1	3,3 ± 1,4	4,2 ± 1,7
Laboratory B	6,5	4,4	7,2
Result of confirmatory test (GCxGC-	MOAH presence confirmed	MOAH presence confirmed	MOAH presence could

MS) by laboratory B	not be confirmed

Example 5. Seven different fish oils analyzed by two different third-party laboratories.

Interpretation. Very marked and inconsistent differences in the levels of individual fractions and total MOAH were found by two third-party laboratories for the same samples.

Product	Laboratory	MOAH (mg/kg)				
		C10-C16	C16-C25	C25-C35	C35-C50	C10-C50
A	E	<1	1.8	<1	<1	2.9
	F	<1	5.9	<1	<1	5.9
B	E	<1	<1	1.4	1.7	3.3
	F	<1	<1	2.6	<1	2.6
C	E	<1	<1	2.8	3.5	6.6
	F	<1	<1	1	<1	1
D	E	<1	<1	1.6	3.5	5.2
	F	<1	<1	2.2	<1	2.2
E	E	<1	<1	<1	<1	1.3
	F	<1	4.6	1.7	<1	6.3
F	E	<1	<1	<1	<1	1.1
	F	<1	<1	3.9	<1	3.9
G	E	<1	1.5	1.1	<1	2.7
	F	<1	6	1.7	<1	7.7

Example 6. The same batch of a refined fish oil analyzed for MOAH content by three different third-party laboratories.

Interpretation. Whereas two laboratories found MOAH below the limit of quantification, a third-laboratory laboratory reports a significant level of MOAH. It is unclear which laboratory is correct, and whether there is even a contamination present which requires mitigation.

Laboratory	MOAH C10-50 (mg/kg)
A	< 1
B	< 1
G	5,5

A high degree of interlaboratory variability is reported in a recent ring test for the EN 16995 2017/DGF-C-VI 22 (20) methods. While the same method needs to be used, each laboratory

will have differences in the way the sample is prepared, for example regarding their protocol for epoxidation, and how integration of the MOAH hump is carried out. The JRC guidance document "Mineral Oil in Infant Formula – Guidelines for Integrating Chromatograms" illustrates how variable hump integration can be. The organization of a periodic ring test in which commercial laboratories can participate, and which includes EPA/DHA omega-3 oil products, is necessary. This will allow laboratories to determine their proficiency. Ultimately, this should lead to a multi-laboratory validation of the EN 16995 2017 and/or DGF-C-VI 22 (20) methods, in which both commercial laboratories and national reference laboratories can participate, in order to determine the real and realistic method precision for edible oils, and which importantly also includes EPA/DHA-rich oils.

3. Choice and availability of laboratories

Ingredient omega-3 oil producers, contract manufacturers, and brands can only obtain information regarding the levels of MOSH/MOAH in their products by submitting samples for analysis to commercial third-party laboratories. Due to the complexities detailed above, none of our member companies have been able to incorporate these analytical methods in-house. Nor do they have access to EU and national reference laboratories, in which methods for MOH analysis have been developed or in which food products are tested by the national food authorities. The third-party laboratories that can analyze EPA/DHA omega-3 oils using the EN 16995 2017/DGF-C-VI 22 (20) methods are located only in Germany, The Netherlands, Switzerland, and France. Our members mostly use Eurofins (Germany), Institut Kirchhoff Berlin (Germany), SGS (Germany), SQTS (Switzerland), Nofalab (The Netherlands) and ITERG (France).

Supply lines are global and typically very long in the omega-3 industry, with fisheries and oil suppliers located in various parts of the world. No laboratories outside of Europe are known to us that can quantify MOSH/MOAH in omega-3 oils, making testing difficult for FBOs outside of Europe, but doing business in the EU. Apart from costs, which can be a challenge for the smaller companies involved, the turnaround times for shipping of samples, coupled with long queues for the laboratory analysis, means the results take many weeks to be received by interested companies.

4. Interference

We note that in the draft implementing regulation amending Regulation (EC) No 333/2007, the performance criteria for official controls require that the method is "Free from matrix or spectral interferences." It is impossible to currently establish such a low LOQ because of matrix interference with the recommended methods EN 16995 2017 and/or DGF-C-VI 22 (20). [1] The various European contract laboratories have made their own modifications to DIN EN 16995 2017 to achieve comparable sensitivity to DGF-C-VI 22 (20); however, they still

[1] BS EN 16995:2017. Foodstuffs. Vegetable oils and foodstuff on basis of vegetable oils. Determination of mineral oil saturated hydrocarbons (MOSH) and mineral oil aromatic hydrocarbons (MOAH) with on-line HPLC-GC-FID analysis.

frequently report challenges with interferences in some omega-3 matrices which necessitate raising the LOQ. Each laboratory reports the employed method in its own manner on testing reports, and method modifications and confirmatory methods have been, or still remain to be, implemented at different velocities by the various laboratories, and are not explained in detail. These methods were validated for vegetable oils and foodstuff on the basis of vegetable oils and are not directly applicable for marine oils, especially unrefined fish/marine oils that have more complex lipid profiles.

GOED estimates that for approximately 10% of EPA/DHA-rich oils, it is impossible to quantify the concentration of MOAH with method EN 16995 2017/DGF-C-VI 22 (20) due to the presence of naturally occurring substances that interfere with the analysis. These substances have similar physicochemical properties as MOAH and cannot be, or can only partially be, separated from MOAH. We believe the matrix interference is caused by naturally occurring terpenes, sterols and process-induced steradienes, and monocyclic aromatic steroid hydrocarbons that coelute with the MOAH fraction.

The current recommended methods for quantifying MOAH (EN 16995 2017) and DGF-C-VI 22 (20) are not able to remove such interferences consistently and selectively in the sample preparation. For some types of oils, such as cod liver oil and tuna oil, the interference can preclude quantification in a significant portion of produced batches, and individual producers can be markedly affected (see examples 1 and 2 in section 2 above). *Interpretation: Enhanced LOQs are assigned to specific samples, dependent on the laboratory, and often not in a logical or consistent manner*. For other oil types, this rate is low, or no interference is observed.

In addition, specific oil types with complex lipid profiles, such as krill oil with a high content of phospholipids (up to 60%), are proving to be very challenging to analyze by third-party testing laboratories. Laboratories already struggle to quantify MOAH in oils containing 1% lecithin.

Multiple laboratories that our members utilize for quality control, such as Eurofins (Germany), Institut Kirchhoff Berlin (Germany), SGS (Germany) and SQTS (Switzerland), are reporting matrix interferences when attempting to quantify MOAH in fish oils and other omega-3-rich oils, necessitating that they raise the LOQ. Such "enhanced" or "raised" LOQs of ≥2.0 mg/kg are warranted when interference is present and can range up to 10 mg/kg, in some cases up to 15 mg/kg, and in rare cases much higher. Sample preparation approaches have improved in the past year by various third-party laboratories, but often this is still not resolving matrix interference; upon confirmatory analyses with GC x GC/TOF-MS, the interference cloud(s) of peaks often still largely overlaps with the MOAH cloud. A targeted analysis cannot be performed because the identity of the natural interferences is also largely unknown. No known analytical method exists that is sensitive enough to discriminate fossil (*i.e.* mineral oil) from natural (recent biogenic) substances.

The above-mentioned presence of analytical interference affects producers and brands disproportionally. From *EFSA's Update of the risk assessment of mineral oil hydrocarbons in food*, it seems that occurrence data hindered by the presence of interferences have not been used. Hence it seems reasonable to conclude that products found to display interferences in

the monitoring analysis, with a resulting need for an enhanced LOQ, will not be used, and certainly not interpreted as having high MOAH levels.

5. Challenges to multiring MOAH removal from EPA/DHA

While traditional chemical and physical refining approaches can reduce the level of MOSH and MOAH in EPA/DHA omega-3 oils, the heavier MOAH fraction (approximately C30-C50) is resistant to removal. While this may be a unique aspect of the omega-3 sector, the precise reason is not known, but points to similar physicochemical properties of multiring MOAH with EPA and DHA, the target fatty acids of interest in our sector. Specific proprietary approaches to remove multiring MOAH likely exist, and new removal technologies may be developed, but these are not available to all producers today. More time is also needed to evaluate new technologies to verify that there are no other adverse impacts, like increases in process contaminants of safety concern such as 3-MCPD/glycidyl esters.

6. Analytical variability and tolerance in maximum limit

Given the high inter- and intra-laboratory variability mentioned above, GOED believes the applied tolerance in any ML set should be at least as great as the analytical variability. We estimate that interlaboratory variability can be as high as 300%; therefore, a putative ML of 2 mg/kg for EPA/DHA omega-3 oils should theoretically allow a tolerance up to 8 mg/kg until the majority of commercial third-party laboratories achieve an interlaboratory variability of max 50%, as is currently employed by the Dutch food authorities in the monitoring of food items.

7. Target compounds

The EFSA Scientific Opinion "Update of the risk assessment of mineral oil hydrocarbons in food" of September 13, 2023 indicates that only MOAH molecules with three or more aromatic rings pose a genotoxic risk to consumers. Imposing regulations without the ability to distinguish between different MOAH species, and those that are genotoxic and those that are not, could lead to unnecessary restrictions on substances that are not proven to be hazardous. GOED has found that finished products (food supplements) containing MOAH do not contain quantifiable levels of polycyclic aromatic hydrocarbons (PAH; four species: benz-a-anthracene, benz-a-pyrene, benzo-b-fluoranthene, and chrysene). See example below.

Example 1. Twenty fish oil retail products were analyzed for both polycyclic aromatic hydrocarbon (PAH) levels and MOAH levels.

Interpretation: While the observed levels of MOAH can vary in a set of EPA/DHA omega-3 oil-containing finished products, the levels of PAH, which are encompassed by the "3-or-more ring" MOAH group (these four PAH species contain 4- or 5 aromatic ring structures), are always below the limit of quantification, i.e. absent.*

Product number	PAH (µg/kg; sum of four species)	MOAH C10-C50 (mg/kg)
A	< 2	< 1
B	< 2	5
C	< 2	18
D	< 2	< 1
E	< 2	1,1
F	< 2	2,2
G	< 2	1,4
H	< 2	13
I	< 2	< 2
J	< 2	< 1
K	< 2	1,1
L	< 2	11
M	< 2	2,7
N	< 2	< 2
O	< 2	32
P	< 2	3,2
Q	< 2	17
R	< 2	< 1
S	< 2	< 1
T	< 2	3,3

* PAH four species: benz-a-anthracene, benz-a-pyrene, benzo-b-fluoranthene, and chrysene (LOQ = 2 µg/kg)

This clearly shows that our products are not unsafe regarding well-studied genotoxic multiring aromatic hydrocarbons. Since PAHs are already covered by Commission Regulation (EU) 2023/915, in our opinion, it would make more sense for the EC to expand the existing regulation and include other known genotoxic PAHs. In light of the ALARA principle in setting a ML, it is more straightforward to invest resources in understanding which additional polycyclic MOAH species are carcinogenic, which are likely to be few, than regulating all MOAH species, most of which likely are devoid of genotoxicity.

8. Other inputs for omega-3 oil processing

We note that existing regulations, such as EU Regulation 10/2011 and 1935/2004, which cover plastic and other materials coming in contact with food, do not currently address the MOAH risk. For this reason, it is challenging for our members to know if their suppliers of food contact materials are supplying MOAH-free materials, which adds another layer of complexity to the issue. No information is furthermore available on technological auxiliaries, such as processing aids necessary to control other contaminants that are removed or controlled in edible oil refining (examples are bleaching earths and activated carbon). This suggests a gap in the comprehensive management of MOAH risks, which should be addressed also before imposing MLs on finished products to ensure a more holistic and effective strategy in managing MOAH risks in the food industry.

9. Absolute intake of EPA/DHA omega-3 oils

GOED would also like to point out that the intake of EPA/DHA omega-3 oils by European consumers is typically 50-fold less than vegetable oils (*manuscript in preparation*). While we know that under the ALARA principle the EC does not consider absolute food intake and bases its regulation on available occurrence data, European consumers that take supplemental omega-3 in the form of EPA/DHA-rich oils consume at most two grams per day, with the median intake being much lower than that.

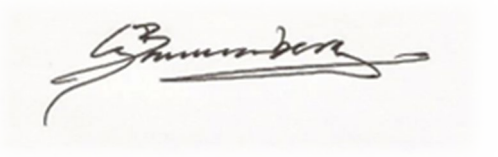
To summarize, we are requesting the following:

- A delayed implementation of the Maximum Limit (ML) for EPA/DHA omega-3 oils for an additional 12 months or until the issues identified in this letter are resolved.
- An allowable tolerance up to 8 mg/kg until the majority of commercial third-party laboratories achieve an interlaboratory variability of max 50%.
- A ring test for both national reference laboratories and commercial laboratories to determine laboratory proficiencies for MOAH quantification in edible oils, including EPA/DHA-rich oils.

We would be happy to engage with the European Commission further regarding any of the points in this letter and could share additional insights specific to our sector.

GLOBAL ORGANIZATION FOR EPA AND DHA OMEGA-3S

Respectfully,



Harry B. Rice, PhD
Vice-President, Regulatory
& Scientific Affairs
harry@goedomega3.com

Gerard Bannenberg, Ph.D.
Director, Technical Compliance &
Outreach
gerard@goedomega3.com

On behalf of the Board of GOED:

Algarithm, Canada

Aker Biomarine, Norway

Amway, USA

BASF, Germany

Bioriginal, Canada

Carlson Laboratories, USA

dsm-firmenich, The Netherlands/ Switzerland

Epax/ Pelagia, Norway

Golden Omega, Chile

Nature's Way Canada, Canada

SGS/Nutrasource, Canada

Olvea, France

Pharma Marine, Norway

Pharmavite, USA

Solutex, Spain

TASA, Peru

Wiley Companies, USA