Technical Guide

for the elaboration of monographs on Fatty oils and Derivatives

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TECHNICAL GUIDE FOR THE ELABORATION OF MONOGRAPHS ON FATTY OILS AND DERIVATIVES AND ON SOME POLYMERS AND SOLVENTS

1. GENERAL

Due to the particular properties of the monographs on fatty oils and derivatives, special guidelines are needed for the different classes of products:

- surfactants like ethoxylated fatty acids, fatty alcohols, glycerides and sorbitan esters of fatty acids, or like sodium laurilsulfate, propylene glycol stearate, sorbitan oleate, sodium cetostearyl sulphate and glycerol monostearate 40-55
- oils, fats and waxes like almond oil and other vegetable oils, hydrogenated vegetable oils, cod-liver oil, hard fat, glycerides, beeswax
- fatty acids, fatty alcohols and their esters/ethers like stearic acid, cetyl palmitate, octyldodecanol, cetostearyl alcohol, cetostearyl isononanoate, ethyl oleate
- polymers
- solvents.

The main target of this technical guide is to obtain harmonised monographs. Therefore for elaborating a new monograph the analytical parameters mentioned in these guidelines should always be taken into consideration and included in the monograph if it is meaningful and convenient.

For a group of chemically identical substances having different molecular masses, different ethoxylation degrees or different concentrations it is recommended to work out a family monograph.

The monographs on fatty oils and derivatives mainly concern excipients. It may happen that an excipient is also used as an active substance, in which case 2 separate monographs may be drafted, due to different requirements. An assay is included in the monograph on the active substance (e.g. omega-3-acid derivatives, fish oils, lauromacrogol 400 etc.)

2. MONOGRAPHS ON SURFACTANTS

2.1. DEFINITION

The following items should be mentioned if meaningful or convenient:

- composition of the fatty acid or fatty alcohol part (see *Macrogol cetostearyl ether* (*1123*) or *Polysorbate 80* (*0428*)
- main component(s) because most of the surfactants are mixtures (see *Macrogol oleyl ether* (*1125*)
- degree of ethoxylation (number of moles of ethylene oxide reacted) or average molecular mass of the macrogol reacted with the fatty part (only macrogol-containing surfactants)
- possible ways of synthesis (e.g. ethoxylation of a fatty acid or reaction of macrogol with the fatty acid, see *Macrogol stearate* (*1134*))
- origin of the fatty part (for example, vegetable)
- percentage content of the main component(s) (see *Glycerol monostearate 40-55* (*0495*))
- reference to the monograph of a constituent used for the production.

2.2. CHARACTERS

The following items should always be mentioned:

- appearance, colour
- solubility (water, organic solvents except chloroform and ether)

The following items should be mentioned if meaningful or convenient:

- viscosity (for liquids only) (*2.2.9*, see *Macrogolglycerol ricinoleate* (*1082*))
- relative density (for liquids only) (*2.2.5*, see *Polysorbate 80* (*0428*))
- freezing point (*2.2.18*) or melting point (*2.2.14* or *2.2.15* or *2.2.60*) or drop point (*2.2.17*)
- refractive index (for liquids only) (*2.2.6*)
- cloud point.

2.3. IDENTIFICATION

The different components of the surfactant (fatty part, macrogol etc.) should be identified if possible. On the other hand more and more analytical methods without chemical reactions should be considered like the (near) infrared spectra (see monograph on *Polysorbate 80*).

Unfortunately these physical methods are not always sufficient to identify completely a surfactant. In such cases the following tests could be considered:

- chromatographic method for fatty acids or fatty alcohols (Examples of methods: thin-layer chromatography see *Macrogol stearyl ether* (*1340*), *gas chromatography* (*2.4.22*) see *Polysorbate 80* (*0428*)
- iodine value to distinguish between saturated and unsaturated substances (*2.5.4*)
- saponification value to distinguish between esters and ethers (*2.5.6*)
- cloud point (see *Nonoxinol 9* (*1454*))
- melting point (*2.2.14* or *2.2.15* or *2.2.60*).

2.4. TESTS

The following tests should be included if meaningful and convenient:

- appearance of solution (*2.2.1* and *2.2.2* e.g. macrogol ethers)
- alkalinity (*Macrogolglycerol hydroxystearate* (*1083*)
- acid value (*2.5.1*)
- saponification value (*2.5.6*. Range or upper limit. Typical example: "Not more than 3.0, determined on 10.0 g")
- iodine value (*2.5.4*. Range or upper limit. Typical example: "Not more than 2.0"). Only included if no test for Composition of fatty acids/alcohols.
- hydroxyl value (*2.5.3*)
- composition of fatty acids (*2.4.22* or *2.2.28*)
- free glycerol (see *Glycerol monostearate 40-55* (*0495*))
- free ethylene glycol or propylene glycol (gel phase chromatography: see *Propylene glycol monopalmitostearate* (*1469*))
- Free macrogol (liquid chromatography: see *Macrogol 15 hydroxystearate* (*2052*)
- free sucrose (liquid chromatography: see *Sucrose monopalmitate* (*2319*)
- free sorbitol
- residual ethylene oxide ("Not more than 1 ppm") and dioxane ("Not more than 10 ppm") (*2.4.25*)

- heavy metals (*2.4.8*) if used during the production
- total ash (*2.4.16*) or sulphated ash (*2.4.14*) after an initial ignition step
- water content (*2.5.12*. Typical example: "Not more than 3.0 per cent, determined on 2.0 g").

2.5. ASSAY

One or two of the following assays could be considered if convenient:

- fatty alcohol composition by gas chromatography (see *Cetostearyl alcohol emulsifying* (*1123*))
- titration (see *Sodium laurilsulfate* (*0098*)
- mono-, di- and triglycerides (gel phase chromatography: e.g. see *Glycerol monostearate 40-55* (*0495*))

2.6. STORAGE

The definitions concerning storage set out in the General Notices (*1*) and in the section on containers (*3.2*) apply here. Generally this section includes the wording:

"Store in a well-filled container / protected from light / under an inert gas".

2.7. LABELLING

See general technical guidelines.

3. MONOGRAPHS ON VEGETABLE OILS, FATS AND WAXES

3.1. TITLE

English/French title: This is the main title, usually derived from the English/French name of the source plant e.g. Almond oil. Additions are: virgin, refined or hydrogenated.

Latin title: This is the subtitle, usually derived from the botanical name of the source plant i.e. the genus (genitive), followed by *oleum* (nominative and singular) e.g. *Amygdalae oleum*. Additions are *virginum raffinatum* or *hydrogenatum*.

3.2. DEFINITION

The following items should be mentioned if meaningful or convenient:

- the complete scientific Latin name of the plant (genus, species variety, author) for plants obtained from the *Kew Index* and its supplements (*International Plant Names Index, IPNI*), and the part of the plant used. The plant names are written in italics
- the means by which the product is obtained e.g. expression, extraction, refining
- addition of additives (for example, antioxidants).

3.3. CHARACTERS

The following items should always be mentioned:

- appearance, colour
- solubility (water, organic solvents, except chloroform and ether).

The following items should be mentioned if meaningful or convenient:

- melting point (*2.2.14* or *2.2.15* or *2.2.60*)
- drop point (*2.2.17*)
- freezing point (*2.2.18*)
- relative density (*2.2.5*)
- refractive index (*2.2.6*).

3.4. IDENTIFICATION

The following tests may be mentioned if meaningful or convenient:

- absorbance (see *Virgin almond oil* (*0261*) and *Refined olive oil* (*1064*))
- hydroxyl value (*2.5.3*)
- iodine value (*2.5.4*); only included if no test for composition of fatty acids/alcohols
- saponification value (*2.5.6*); only included if no test for composition of fatty acids/alcohols
- chemical identification reactions
- identification of fatty oils by thin-layer chromatography (*2.3.2)*
- composition of fatty acids by gas chromatography (*2.4.22*)

Concerning virgin and refined oils, the identification section is organised according to the following criteria:

— **a thin-layer chromatography is preferred**

• thin-layer chromatography (*2.3.2*) + melting point (for a solid product)

• thin-layer chromatography (*2.3.2*) + a value that allows differentiation between similar oils

— when a thin-layer chromatography is not convenient

• cross-reference to the test for composition of fatty acids (*2.4.22*) is sufficient when there is no risk of confusion between oils

• cross-reference to the test for composition of fatty acids (*2.4.22*) + melting point (for a solid product)

• cross-reference to the test for composition of fatty acids (*2.4.22*) + a value allowing for differentiation between similar oils

— if the thin-layer chromatography test and the test for composition of fatty acids are not enough

• composition of triglycerides

3.5. TESTS

*The limits proposed by the "*Codex Alimentarius" *should be considered as far as possible.*

The following tests should be included if meaningful and convenient:

- optical rotation (*2.2.7*) (see castor oils)
- melting point (*2.2.15*) for waxes
- drop point (*2.2.17*) for waxes
- absorbance (*2.2.25*)
- alkaline impurities in fatty acids (*2.4.19*)
- acid value (*2.5.1*)
- hydroxyl value (*2.5.3*)
- iodine value (*2.5.4*); only included if no test for composition of fatty acids
- peroxide value (*2.5.5*)
- saponification value (*2.5.6*); only included if no test for composition of fatty acids
- unsaponifiable matter (*2.5.7*)
- chemical reactions
- composition of fatty acids (*2.4.22*)
- sterols in fatty oils (*2.4.23*)
- water content, semi-micro method (*2.5.12*) or coulometric method (for oils) or loss on drying (*2.2.32*)
- nickel by atomic absorption spectrometry (*2.4.31*)
- total ash (*2.4.16*) or sulphated ash (*2.4.14*) after an initial ignition step

3.6. STORAGE

The definitions concerning storage set out in the General Notices (*1*) and in the section on containers (*3.2*) apply here. Generally this section includes the wording:

"Store in a well-filled container / protected from light / under an inert gas"

And for hydrogenated oils:

“Store in a well-filled container, protected from light”.

3.7. LABELLING

See general technical guidelines.

4. MONOGRAPHS ON ANIMAL OILS, FATS AND WAXES

4.1. TITLE

The English/French and Latin titles are derived from a description of the product e.g. *Wool fat / Graisse de laine (Adeps lanae)* (*0134*), *White Beeswax / Cire d'abeilles blanche (Cera alba)* (*0069*), *Cod-liver oil / Huile de foie de morue (Iecoris aselli oleum)* (*1192*).

4.2. DEFINITION

The following items should be mentioned if meaningful or convenient:

- the complete scientific Latin name of the animal (genus, species variety, author) and the part of the animal used. The animal names should be written in italics
- the means by which the product is obtained
- where appropriate: minimum and maximum contents of active substances (for example, vitamins in Cod-liver oil)
- mention of additives (for example, antioxidants)

4.3. CHARACTERS

The following items should always be mentioned:

- appearance, colour
- solubility (water, organic solvents, except chloroform and ether).

The following items should be mentioned if meaningful or convenient:

- melting point (*2.2.14* or *2.2.15* or *2.2.60*)
- drop point (*2.2.17*)
- freezing point (*2.2.18*)
- relative density (*2.2.5*)
- refractive index (*2.2.6*).

4.4. IDENTIFICATION

The following tests may be mentioned if meaningful or convenient:

- assay of an active substance (see *Cod-liver oil* (*1192*))
- chemical identification reactions
- chromatographic methods (thin-layer chromatography)
- composition of fatty acids (*2.4.22*)
- positional distribution (β (2)-acyl) of fatty acids by NMR (see *Salmon oil, farmed* (*1910*)).

4.5. TESTS

The following tests should be included if meaningful and convenient:

- appearance (*2.2.1* and *2.2.2*) (see *Fish oil rich in omega-3 acids* (*1912*))
- melting point (*2.2.15*) for waxes
- drop point (*2.2.17*) for waxes
- absorbance (*2.2.25*) (see Omega-3 acids ethyl esters (*1250*, *2063*))
- alkaline impurities in fatty acids (*2.4.19*)
- acid value (*2.5.1*)
- ester value (*2.5.2*) for Beeswax
- hydroxyl value (*2.5.3*)
- iodine value (*2.5.4*); only included if no test for composition of fatty acids
- peroxide value (*2.5.5*)
- anisidine value (*2.5.36*) (see *Cod-liver oil* (*1192*), omega-3 acids ethyl esters (*1250*, *2063*))
- saponification value (*2.5.6*); only included if no test for composition of fatty acids/alcohols

- unsaponifiable matter (*2.5.7*)
- chemical reactions
- composition of fatty acids (*2.4.22*)
- chromatographic methods (size-exclusion chromatography, see omega-3 acids ethyl esters (*1250*, *2063*))
- water content, semi-micro method (*2.5.12*) or coulometric method or loss on drying (*2.2.32*)
- total ash (*2.4.16*) or sulphated ash (*2.4.14*) after an initial ignition step.

4.6. ASSAY

- Nuclear magnetic resonance spectrometry (see *Salmon oil, farmed* (*1910*)).

4.7. STORAGE

The definitions concerning storage set out in the General Notices (*1*) and in the section on containers (*3.2.*) apply here. Generally this section includes the wording:

"Store in a well-filled container / protected from light / under an inert gas".

4.8. LABELLING

- the names and concentrations of vitamins are stated on the label (for example, vitamins in Cod-liver oil), if appropriate.

5. MONOGRAPHS ON FATTY ACIDS, FATTY ALCOHOLS AND THEIR ESTERS/ETHERS

5.1. DEFINITION

The following items should be mentioned if meaningful or convenient:

- composition of the fatty acid / fatty alcohol / ester / ether
- synthetic method or method of manufacture
- origin of the fatty acid or/and of the fatty alcohol (for example, vegetable, animal, synthetic)
- mention of additives (for example, antioxidants)
- percentage content of the main components(s).

5.2. CHARACTERS

The following items should always be mentioned:

- appearance, colour
- solubility (water, organic solvents except chloroform and ether)

The following items should be mentioned if meaningful or convenient:

- relative density (*2.2.5*)
- refractive index (*2.2.6*)
- melting point (*2.2.14* or *2.2.15* or *2.2.60*)
- drop point (*2.2.17*).

5.3. IDENTIFICATION

- infrared absorption spectrophotometry (*2.2.24*)
- acid value (*2.5.1*) for acids

- hydroxyl value (*2.5.3*) for alcohols; only included if no test for composition of fatty alcohols
- iodine value (*2.5.4*) to distinguish between saturated and unsaturated substances; only included if no test for composition of fatty acids
- saponification value (*2.5.6*) for esters
- chemical reactions
- chromatographic methods by thin-layer chromatography (*2.3.2*), gas chromatography (*2.2.28, 2.4.22*) or liquid chromatography (*2.2.29*).

5.4. TESTS

The following tests should be included if meaningful and convenient:

- appearance of the solution (*2.2.1* and *2.2.2*)
- alkaline impurities (for alcohols and esters)
- acid value (*2.5.1*)
- hydroxyl value (*2.5.3*); only included if no test for composition of fatty alcohols
- iodine value (*2.5.4*); only included if no test for composition of fatty acids
- peroxide value (*2.5.5*)
- saponification value (*2.5.6*); only included if no test for composition of fatty acids/alcohols
- chemical reactions
- nickel by atomic absorption spectrometry (*2.4.31*) if used; only for products not obtained by distillation
- water content (*2.5.12*)
- total ash (*2.4.16*) or sulphated ash (*2.4.14*) after an initial ignition step.

5.5. ASSAY

The following assays should be considered if convenient:

- fatty acid content by gas chromatography (*2.4.22)*
- fatty alcohol content by gas chromatography (*2.2.28*)

- ester content by liquid chromatography (*2.2.29*)
- gel phase chromatography.

5.6. STORAGE

The definitions concerning storage set out in the General Notices (*1*) and in the section on containers (*3.2)* apply here. Generally this section includes the wording:

“Store in a well-filled / airtight container / protected from light / under an inert gas”.

5.7. LABELLING

See general technical guidelines.

6. MONOGRAPHS ON POLYMERS

6.1. DEFINITION

The following items should be mentioned if meaningful or convenient:

- type of polymer: block polymer, homopolymer, copolymer etc.
- means by which the product is obtained
- mean relative molecular mass (see *Poly(vinyl acetate), dispersion 30 per cent (2152)*)
- percentage content
- possible addition of stabilisers (see *Macrogols (1444)*, *Poly(vinyl acetate), dispersion 30 per cent (2152)*).

6.2. CHARACTERS

The following items should always be mentioned:

- appearance, colour
- solubility (water, organic solvents except chloroform and ether)

The following item should be mentioned if meaningful or convenient:

- melting point (see *Poloxamers (1464)*).

6.3. IDENTIFICATION

The following tests should be included if meaningful and convenient:

- infrared absorption spectrophotometry (*2.2.24*)
- average relative molecular mass (see *Poloxamers (1464)*)
- oxypropylene : oxyethylene ratio (see *Poloxamers (1464)*)
- identification reactions, e.g. reaction of acetyl
- viscosity (*2.2.9*) (*Macrogols (1444)*).

6.4. TESTS

The following tests should be included if meaningful and convenient:

- appearance of solution (*2.2.1* and *2.2.2* for example, Macrogols, Poloxamers)
- acidity or alkalinity
- pH (*2.2.3*)
- hydroxyl value (*2.5.3*)
- freezing point (*2.2.18*)
- residual monomer content (ethylene oxide, propylene oxide, vinyl acetate etc.)
- residual solvents and volatile organic impurities (dioxan, acetic acid etc.)
- propylene oxide: ethylene oxide ratio by nuclear magnetic resonance spectrometry (*2.2.33*)
- average relative molecular mass
- povidone (stabiliser)
- acetic acid, by liquid chromatography (*2.2.28*)
- heavy metals (*2.4.8*) if used during the production
- water content (*2.5.12*) or residue on evaporation
- total ash (*2.4.16*) or Sulphated ash (*2.4.14*) after an initial ignition step.

6.5. ASSAY

An assay could be considered if convenient.

6.6. STORAGE

The definitions concerning storage set out in the General Notices (*1*) and in the section on containers (*3.2*) apply here. Generally this section includes the wording:

“Store in an airtight container”.

6.7. LABELLING

See general technical guidelines.

7. MONOGRAPHS ON SOLVENTS

7.1. DEFINITION

The following items should be mentioned if meaningful or convenient:

- chemical composition
- the means by which the product is obtained
- percentage content

7.2. CHARACTERS

The following items should always be mentioned:

- appearance, colour
- solubility (water, organic solvents except chloroform and ether)
- relative density (*2.2.5*).

7.3. IDENTIFICATION

The following tests should be included if meaningful and convenient:

- infrared absorption spectrophotometry (*2.2.24*)
- saponification value (*2.5.6*) for esters (see Isopropyl myristate (*0725*))
- relative density (*2.2.5*)
- refractive index (*2.2.6*)
- boiling point (*2.2.12*)
- chemical reactions (see *Propylene glycol* (*0430*)).

7.4. TESTS

The following tests should be included if meaningful and convenient:

- appearance or Appearance of solution (*2.2.1* and *2.2.2* e.g. *Propylene glycol* (*0430*))
- relative density (*2.2.5*)
- refractive index (*2.2.6*)
- acidity or alkalinity, or acid value (*2.5.1*)
- iodine value (*2.5.4*)
- saponification value (*2.5.6*)
- viscosity (*2.2.9*) (see *Isopropyl myristate* (*0725*))
- oxidising substances
- reducing substances
- heavy metals (*2.4.8*) if used during the production
- water content (*2.5.12*)
- total ash (*2.4.16*) or sulphated ash (*2.4.14*)

7.5. ASSAY

An assay could be considered if convenient, generally by gas chromatography (*2.2.28*).

7.6. STORAGE

The definitions concerning storage set out in the General Notices (*1*) and in the section on containers (*3.2*) apply here. Generally this section includes the wording:

“Store protected from light / in an airtight container”.

7.7. LABELLING

See general technical guidelines.