GUIDANCE ON ESSENTIAL OILS

in cosmetic products

Consumer Health Protection Committee (CD-P-SC)

2016

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Guidance on essential oils in cosmetic products

European Directorate for the Quality of Medicines & HealthCare

Guidance on essential oils in cosmetic products is published by the European Directorate for the Quality of Medicines & HealthCare of the Council of Europe (EDQM).

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Page layout and cover: EDQM

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CONTENTS

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1. Introduction

Essential oils have become an integral part of everyday life. They are used in a great variety of ways – from flavouring agents to the essence of cosmetic products. Many aromatherapists and laymen consider natural essential oils to be completely safe. This is based on the misconception that all herbs are safe because they are natural. The toxicity of essential oils can also be entirely different to that of the herb, not only because of their high concentration, but also because of their physicochemical properties. Essential oils, as products of distillation for example, are mixtures of mainly low-molecular-weight chemical substances which, combined with their lipophilicity, results in an ability to pass across membranes very efficiently.

Many essential oils that are considered to be nontoxic can have deleterious effects on certain cohorts of people. These effects can be influenced by previous sensitisation to a given essential oil, a group of essential oils containing similar components, or some adulterant in the essential oil. The degree of toxicity can also be influenced by the age of the person. Owing to the influence of age on skin structure and metabolism, the very young and the elderly are particularly vulnerable to harmful effects of products applied to the skin. With this in mind, it is prudent to be cautious in using essential oils in topically applied cosmetic products.

This document aims to address the quality factors and risks associated with essential oils in cosmetic products. More specifically, section 3 aims to highlight the importance of the quality of essential oils and of the starting materials from which they are obtained; section 4 aims to provide recommendations on the risk assessment of essential oils and the potential implications when including them in cosmetic products.

This document is intended for operators and, in particular, responsible persons in the cosmetics industry whose obligations are to ensure the safety of cosmetic products in accordance with European and national cosmetic legislative frameworks. This includes, but is not limited to, operators who manufacture, contract the manufacture or import cosmetic products containing essential oils.

Furthermore, the document is intended to support safety assessors carrying out the safety assessment of cosmetic products, as well as competent authorities in reviewing these assessments.

Unfortunately, essential oils are not defined in the cosmetic legislation. They may be composed of various substances – typically mixtures of liquid, volatile and fat soluble plant ingredients or of synthetic aromatic substances with a characteristic fragrance. In contrast to fatty oils, essential oils evaporate. The mixtures consist of a number of chemical compounds most of which, chemically, are terpenes and their derivatives [1].

Whilst there is no cosmetic product definition for essential oils, the most developed definition in terms of application to public health has come from the medicinal product world. The Commission of the European Pharmacopoeia has adopted a definition of an essential oil [2], which is very similar to that of the International Organization for Standardisation (ISO 9235: 2013) standards on aromatic natural raw ingredients [3]:

> *Odorous product, usually with a complex composition, obtained from a botanically defined plant raw material by steam distillation, dry distillation, or a suitable mechanical process without heating. Essential oils are usually separated from the aqueous phase by a physical process that does not significantly affect their composition.*

The Pharmacopoeia goes on to describe how essential oils may be subjected to a suitable subsequent treatment. Thus an essential oil may be commercially known as deterpenated, desesquiterpenated, rectified or 'x'-free.

- A *deterpenated essential oil* is an essential oil from which monoterpene hydrocarbons have been removed, partially or totally.
- A *deterpenated and desesquiterpenated essential oil* is an essential oil from which the mono- and sesquiterpenic hydrocarbons have been removed, partially or totally.
- A *rectified essential oil is an essential oil* that has been subjected to fractional distillation to remove certain constituents or modify the content.

- An *'x'-free essential oil* is an essential oil that has been subjected to partial or complete removal of one or more constituents.

Only essential oils that satisfy this definition (synthetic substances are not included) are considered in this document; however from a toxicological point of view, there is no difference between a natural and a synthetic molecule.

From the outset, it should also be noted that this document specifically relates to the use of essential oils in cosmetic products. It should be borne in mind that where an ingredient's concentration, function or claim comes under the scope of Directive 2001/83/EC, as amended, relating to medicinal products, it is therefore not a cosmetic product. This is particularly relevant where there is a borderline between essential oil ingredients used in cosmetic products and those used in herbal medicinal products.

2. Regulatory context

2.1. Cosmetic Regulation (EC) No. 1223/2009 as amended

In the European Union, cosmetic products are regulated by the Cosmetics Regulation (EC) No. 1223/2009, as amended [4], for which certain provisions specifically address the use of essential oils in cosmetic products, most notably in Annex II and Annex III. The onus is on the responsible person to ensure that products they place on the market meet these regulatory requirements. The Cosmetics Regulation requires responsible persons to ensure that a cosmetic product has undergone a safety assessment on the basis of the relevant information prior to placing the cosmetic product on the market. A safety report has to be set up in accordance with Annex I. Guidelines on Annex I are laid down in the Commission Implementing Decision 2013/674/EU. There is also further supplementary information relevant to cosmetic product ingredients found in the guidance in the Council of Europe publication relating to ingredients used in cosmetics [5].

Annex II to Regulation (EC) No. 1223/2009, as amended, lists substances which are prohibited for use in cosmetic products. Among substances listed in this annex are:

- plant ingredients which are prohibited in cosmetic products, regardless of the function;
- plants and their compounds which are prohibited in cosmetic products for a given function (perfume ingredients);
- substances which are prohibited in cosmetic products unless they are naturally present in extracts, and essential oils which are subject to concentration limits.

In general the non-intended presence of a small quantity of prohibited substance, stemming from natural ingredients for example, is permitted when it is technically unavoidable in good manufacturing practice provided that such presence is safe (Article 17 of the Cosmetics Regulation).

Annex III of Regulation (EC) No. 1223/2009, as amended, lists substances that cosmetic products must not contain except subject to the restrictions laid down. In 2016, this annex includes twenty-six substances, known as fragrance allergens, subject to mandatory labelling conditions due to their allergenic potential. Their presence in cosmetic products must be mentioned on the packaging when their concentration exceeds the threshold of 10 ppm (0.001 %) in leave-on products and 100 ppm (0.01 %) in rinse-off products.

It should be noted that according to Article 15 of Regulation (EC) No. 1223/2009, as amended, the use in cosmetic products of substances classified as carcinogenic, mutagenic or toxic for reproduction, of category 1A, 1B, 2, under Part 3 of Annex VI to Regulation (EC) No. 1272/2008, is prohibited. However, a substance classified in category 1A or 1B may be used in cosmetic products where the substance has been evaluated by the Scientific Committee on Consumer Safety (SCCS) and found safe for use in cosmetic products, and other conditions laid out in article 15 paragraph 2 are fulfilled. A substance classified in category 2 may be used in cosmetic products where the substance has been evaluated by the SCCS and found safe for use in cosmetic products without fulfilling any additional criteria.

The SCCS published an opinion on fragrances allergens in cosmetic products in June 2012 [6]. In this opinion, essential oils and effects as contact allergens in humans are evaluated.

2.2. Examples of specific national legislation and recommendations

- France:
  - Recommendations regarding essential oils quality criteria (May 2008)
  - Recommendations for the risk assessment associated with the use of essential oils in cosmetic products (October 2010)
  - Recommendations to manufacturers and responsible persons for the placing on the market of cosmetic products containing terpenoids: camphor, eucalyptol, menthol (August 2008).
- Germany:
  - The Federal Institute for Risk Assessment recommended the following [1]: maximum concentration of 1 % of camphor, eucalyptus oil, menthol or methyl saliculate in leave-on products and a maximum concentration of 5 % of camphor, 4 % of menthol and 2.5 % of methyl salicylate in rinse-off products.
  - The Federal Institute for Risk Assessment (BfR) has published an opinion on tea tree oil recommending a concentration limit of 1 % for tea tree oil in cosmetic products.
- Switzerland: The Swiss legislation on cosmetics has fixed a maximal concentration of 3.0 % essential

oils (alone or in mixture) in leave-on products (see Annex 3, Ordinance on cosmetics, SR 817.023.31). This maximal concentration helps to delimitate cosmetics and medical products.

2.3. Recommendations of the Council of Europe

The Council of Europe has published three volumes of recommendations concerning the use of plants and plant-based preparations used as ingredients in cosmetic products, as increasing numbers of plant-based cosmetic products have been placed on the market [7-9]. These are in addition to the publication relating to a safety survey of ingredients used in cosmetic products [5] and the recommendation to avoid the use of camphor, eucalyptol or menthol in cosmetic products for infants.

The volumes contain a number of datasheets on plant and plant preparations that have been evaluated by the Council of Europe's Committee of Experts on Cosmetic Products. The entries are classified into three categories: plants which do not present a health hazard; those for which further information is needed; and those which may pose a health risk and are not recommended for use in cosmetic products.

Even though there is a long history of use of natural raw materials, such as plants and plant preparations, in cosmetic products, the Council of Europe's Committee of Experts on Cosmetic Products highlighted the fact that some of the raw materials contain substances with significant activity, which could be potentially harmful for consumers. Therefore it is necessary to take into consideration the risks that these substances could present to consumers when evaluating the overall safety of a cosmetic product.

The Council of Europe has also published recommendations concerning the use of camphor, eucalyptol and menthol [10].

2.4. Recommendations of the International Fragrance Association (IFRA)

The International Fragrance Association (IFRA) represents the collective interests of its members and supports those of the finished fragrance products community. Membership is open to associations of fragrance manufacturers from all countries/regions, and currently includes members from Asia/Pacific, Europe and the Americas. All IFRA members have committed to comply with the IFRA Code of Practice which aims to provide recommendations for good operating practice and guidelines on fragrance ingredient safety assessment, and includes fragrance safety standards which may limit or ban the usage of certain fragrance materials. The IFRA Code of Practice is accessible at http://www.ifraorg.org/.

The IFRA Scientific Committee collects and makes available data for the safety evaluation of fragrance ingredients. As many fragrances contain essential oils and their components, this information should be taken into account by operators incorporating essential oils into cosmetic products.

3. Quality of essential oils

The safe use of essential oils in cosmetic products depends on both the quality of raw materials used and the extraction method by which the neat essential oil is produced. Essential oils should have specific physical and chemical characteristics identified and be stored in well-filled, airtight containers, protected from light.

The physical, organoleptic, chemical and chromatographic characteristics of essential oils are set globally through various ISO standards. There are also ISO standards relating to the nomenclature and the general rules for packaging, conditioning and storing essential oils [11-13].

3.1. Plant raw materials

According to the monograph of the European Pharmacopoeia [2], the plant raw material must be fresh, wilted, dry, whole, bruised or powdered, except for fruits from the *Citrus* genus that must always be processed fresh.

3.1.1. *Botanical name*

The origin of the plant must be precisely defined by the scientific botanical name according to the International Code of Nomenclature for Cultivated Plants rules. The international name of a plant, expressed in Latin, includes the genus name followed by the species name, and the initial or abbreviation of the botanist who first described the plant in question. Where appropriate, it is completed by the subspecies or variety name. The botanical family is usually specified. The accuracy of the name is significant. Differences in chemical composition can occur depending on the botanical origin [14].

An example of a scientific botanical name from the Lamiaceae family would be *Lavandula angustifolia* Mill., in which *Lavandula* refers to the genus, *angustifolia* refers to the species and Mill refers to the botanist's name (Miller). Further examples can be found below.

Genus

E.g.: *Lavandula* and *Mentha*.

Species

Two very similar species, from the same genus, may give different chemical composition of essential oil.

E.g.: True lavender (*Lavandula angustifolia* Mill.); Spike lavender (*Lavandula latifolia* Medik.).

In most cases, each species has a unique chemical profile but it is possible that two species are sources of essential oils of very close compositions.

E.g.: Anise (*Pimpinella anisum* L.); Chinese star anise (*Illicium verum* L.).

Subspecies

A species will in some cases have a number of subspecies.

E.g.: Bergamot (*Citrus aurantium* L. ssp *bergamia* (Wight & Arnott) Engler); Bitter orange (*Citrus aurantium* ssp *aurantium* L.).

Variety

Within a species, there may be varieties with different compositions of essential oils.

E.g.: the species basil (*Ocimum basilicum*) is morphologically and chemically very heterogeneous and is divided into many varieties which are difficult to differentiate (*O. basilicum* var. *basilicum*, *O. basilicum* var. *misshapen* Benth., *O. basilicum* var. *glabratum* Benth.)

Because of possible confusion due to the existence and/or current use of many synonyms, it is necessary to refer to ISO standard 4720: 2009 [12], which gives a list of the botanical nomenclature of plants used for the production of essential oils with the common names of essential oils in English and French. This standard also includes an alphabetical index of common names of essential oils.

3.1.2. *Conditions for the production of the plant raw material*

As growing conditions, harvesting, drying, milling and storage have an impact on the quality of the plant, which in turn may affect the quality of the essential oil, these factors need to be considered.

Plant raw materials are obtained from either gathering or harvesting plants; the latter can be grown from seedlings or cuttings. Plant raw materials should be, as far as possible, free from impurities such as dirt, dust, and fungal infections or animal contamination. They should show no sign of rot or damage.

The wild state or culture conditions and environmental factors play a significant role, not only on the quantitative but also qualitative aspects of the constituents produced by the plant. Therefore it is essential that information regarding the geographical and environmental conditions and production (e.g. use of pesticides) is available. Other parameters such as the exact location of culture, altitude, nature and degree of fertilisation, the wilderness or cultivated plant, its stage of vegetation should also be taken into account. Over time (seasons, months or days) biosynthesis may cause a plant raw material to contain significantly more or less of some metabolites.

In order to inhibit enzyme activity after harvest, which can cause the degradation of some constituents, and to prevent microbial growth, the plant raw material must undergo either immediate distillation or careful drying. For every treatment step that a plant raw material is subject to it is necessary to show that it does not alter the plant constituents or leave harmful residues.

3.1.3. *Part of plant used*

Essential oils exist almost exclusively in higher plants. The genera capable of developing the constituents present in an essential oil are distributed in a limited number of families (e.g. *Apiaceae*, *Asteraceae*, *Cupressaceae*, *Lamiaceae*, *Lauraceae*, *Myrtaceae*, *Poaceae*, *Rutaceae*, etc.).

The essential oils can be accumulated in all types of plant organs but mainly come from the flower and leaf components. Some examples are outlined below;

- flowers (orange, rose, lavender)
- leaves (citronella, eucalyptus, bay laurel)
- bark (cinnamon)
- woods (rosewood, camphor, sandalwood)
- roots (vetiver)
- rhizomes (curcuma, ginger)
- dried fruits (anise, star anise, parsley)
- seeds (nutmeg).

In some cases all the plant organs of the same species may contain essential oils; however, the qualitative and quantitative composition may vary depending on the location of these organs in the plant.

Biosynthesis and accumulation of aromatic molecules are usually associated with the presence of specialised histological structures such as glandular trichomes, secretory cells, secretory cavities, resin ducts, etc. that are often located on or near the surface of the plant [15].

3.1.4. *Accuracy of chemotype*

For any botanical species there may be several chemotypes that have slight differences in biosynthetic pathways. This phenomenon has been well studied for thyme (*Thymus vulgaris* L.) for which there are at least seven different chemotypes, such as alpha-terpineol, carvacrol, cineole, geraniol, sabinene hydrate, linalool, thymol [16].

It is therefore essential for some species to have information relating to the specific chemotype as it can determine the activity and/or toxicity of the essential oils present.

3.1.5. *Identification*

The identity of the initial plant raw material is required to ensure traceability through to the use in cosmetic products. This identity can be achieved either through the provision of licences (if applicable) or documented commitments from the supplier or through one or more of the techniques described below:

- macroscopic botanical characteristics: comparison of the plant raw material with a reference description to allow for rapid identification of the substances;
- microscopic botanical characteristics: microscopic examination of the plant, to search for and identify specific or dominant characters. This examination would enable operators to identify the presence of foreign elements;
- thin layer chromatography or gas chromatography: the chromatogram of the test solution obtained by extraction is compared to a control solution comprising preferably two reference substances (TLC), or to a chromatographic profile (GC).

- The characterisation of the chemotype should be made after identification of the major constituents in the essential oil under analysis.

Additional testing included in the analysis of the plant raw material may include the determination of total ashes, loss on drying or water content (determined by distillation).

Other quality factors relating to pesticide residues and microbiological quality (number and types of micro-organisms) should be verified.

3.2. Essential oil

3.2.1. *Method for extracting essential oils*

The choice of method for extracting the essential oil depends on the original state and the characteristics of the plant raw material.

The ratio of essential oil to plant raw material can be highly variable depending on the plants and can range from 0.015 % to over 20 % [17]. To give an example of this variation 1.5 g of lemon balm essential oil is obtained from 10 kg of fresh lemon balm leaves whereas 2.2 kg of clove essential oil is obtained from 10 kg of cloves.

The extraction method determines characteristics of the essential oil such as viscosity, colour, solubility, volatility, and can cause enrichment or depletion of some components. The extraction methods described below are detailed in the European Pharmacopoeia [2].

Steam distillation

The essential oil is produced by the passage of steam through the plant raw material in a suitable apparatus. The steam may be introduced from an external source or generated by boiling water below the raw material or by boiling water in which the raw material is immersed. The steam and oil vapours are condensed. The water and essential oil are then separated by decantation.

Dry distillation

The essential oil is produced by high-temperature heating of stems or barks in a suitable apparatus without the addition of water or steam.

Mechanical process

The essential oil is produced by a mechanical process without any heating, usually known as 'cold-pressing'. It is mainly applied to *Citrus* fruits and involves the expression of the oil from the pericarp and subsequent separation by physical means. The conventional method of 'cold-pressing' requires an abrasive action to be applied to the entire surface of the fruit under a stream of water. After removal of solid waste, the essential oil is separated from the aqueous phase by centrifugation. Most industrial facilities actually allow simultaneous or sequential production of fruit juice and essential oil.

3.2.2. *Physicochemical characteristics*

Essential oils are typically volatile substances which are liquid at room temperature; this differentiates them from so-called fixed oils. They are somewhat coloured and their density is generally lower than that of water. They have a high refractive index and most rotate polarised light. They are soluble in lipids and common organic solvents and can be distilled with steam. Essential oils are very sparingly soluble in water.

Essential oils are complex mixtures of various constituents in variable concentrations within defined limits. These constituents mainly, but not exclusively, belong to two groups characterised by distinct biogenetic origins: terpenoids, and substances biosynthesised from shikimic acid giving rise to phenylpropane derivatives.

The individual monographs of the European Pharmacopoeia [2] give specific detail on the physicochemical characteristics of each essential oil.

3.2.3. *Identification and chromatographic analyses*

The analysis of essential oils to identify each of the constituents and the test for possible falsifications can be performed using techniques such as gas chromatography on polar, apolar or chiral stationary phases, coupled with mass spectrometry or Fourier transform infra-red (FTIR) detection. Isotopic analysis, for example the measurement of $^{13}C/^{12}C$ or $^{18}O/^{16}O$ ratios can also contribute to testing for frauds. The bibliography [18-26] illustrates some techniques for testing and assaying molecules suspected of being allergenic.

However, routinely and according to the standard guidelines such as the European Pharmacopoeia and the ISO standards, the quality assessment of essential oils is performed by measuring a certain number of indexes and by simple chromatographic analyses. Some examples are outlined below:

- Physical indexes: relative density, refractive index, optical rotation, freezing point, evaporation residue, solubility in ethanol.
- Chemical values: acid value, peroxide value.
- Chromatographic analyses: thin layer chromatography, high performance liquid chromatography (HPLC) for furocoumarins of *Citrus* essential oils, gas chromatography (Pharmacopoeia, ISO) which is the method of choice to obtain the chromatographic profile of the essential oil.

The chromatographic profile of an essential oil performed under specific conditions (capillary column, split or splitless injection mode, flame ionisation detector, preliminary qualification of the installation with a mix of nine compounds test), allows analysts to obtain a reproducible estimate of the different characteristic constituents in the essential oil using a standardised method.

In the case of a finished product containing an essential oil among other components, the assay of the constituents

to be taken into account is based on a calibration method requiring the injection of a standard solution containing each of these constituents at known concentrations.

3.2.4. *Conservation and storage conditions*

Operators should be aware of the relative instability of the constituents in an essential oil and care should be taken to ensure quality during storage.

Signs of degradation can be easily identified by a number of means such as;

- measuring chemical indices
- determining physical characteristics (index of refraction, optical rotation, miscibility with ethanol)
- chromatographic analysis

The consequences of insufficient conservation are numerous, for example, photoisomerisation, photocyclisation, oxidative cleavage, peroxidation and decomposition of alcohols and ketones, thermal isomerisation, hydrolysis and transesterification.

Degradation can change the properties and potentially jeopardise the safety of the essential oil. In order to avoid such degradation, essential oils should be stored in a clean, dry container which is aluminium glazed, stainless steel or anti-actinic tinted glass and which is almost entirely filled and sealed tightly. The air space in the container could be filled with nitrogen or another inert gas. Storage instructions should indicate that the container must be stored away from heat and light. When storing a cosmetic product containing an essential oil, these precautions should be considered. In addition, serious incompatibilities may exist with some types of plastic packaging and this should also be considered.

In some cases, a suitable antioxidant may be added to the essential oil. In this case, the additive is to be mentioned at the time of the sale or use of the essential oil.

The ISO/TS standard 210: 2014 [13] outlines general rules for packaging, conditioning and storage of essential oils.

4. Risk assessment of essential oils in cosmetic products

It is of the utmost importance to remember that the risk assessment of essential oils in cosmetic products must be in compliance with Annex I of the Cosmetic Regulation (EC) No. 1223/2009, as amended, and the Guidelines on Annex I according to the Commission Implementing Decision 2013/647/EU.

Essential oils are very interesting natural plant products and among other qualities they possess various biological properties. Because essential oils are mixtures of volatile organic substances of known chemical structure that react, either singly or in combination, with biomolecules (proteins, etc.) to produce biological responses, it should be possible to relate the intake of doses of these substances to the observed toxicity.

It is often assumed that essential oils are not dangerous because they are obtained from plant raw materials. Certain essential oils may, however, in a dose-dependent manner, cause skin reactions or irritate the eyes and mucous membranes; these include oils of Ceylon cinnamon, exotic basil, peppermint, clove, niaouli, thyme, marjoram, savory and lemon grass. Symptoms may remain for some days after skin contact with the product. Essential oils, for example, used in deodorant spray, can also promote the onset of asthmatic attacks. Accidental oral ingestion of essential oils can cause severe poisoning, leading – depending on dose – to coma or even death. Some essential oils such as lemon, bergamot and bitter orange are phototoxic.

On account of the complexity of these natural products, the toxicological and biochemical testing of an essential oil should take into account the sum of its constituents which can act in an additive, synergistic or in an antagonistic way with one another. Fundamentally, it is the interaction between one or more molecules in the essential oil and macromolecules that yields the biological response, regardless of whether it is a desired functional effect such as a pleasing smell or a potential toxic effect. Attention is drawn to the joint opinion from the Scientific Committee on Health and Environmental Risks, the Scientific Committee on Emerging and Newly Identified Health Risks and the Scientific Committee on Consumer Safety published in 2011 relating to the toxicity and assessment of chemical mixtures [27].

The chemical constitution of an essential oil is fundamental to understanding factors affecting its safety in a cosmetic product. Risk assessments related to the use of an essential oil as an ingredient in cosmetic products must comply with the cosmetic product assessment process recommended by the SCCS [28] in addition to the legislative basis for the assessment of the safety of a cosmetic product according to Annex I of the Cosmetics Regulation detailed in its product information file or the relevant national legislation. Guidance on the cosmetic product safety report (i.e. Annex I) was published in November 2013 [29].

However, due to the complex nature of essential oils, which are generally composed of mixtures of many substances, appropriate supportive or alternative methodologies may be needed. This section presents possible approaches for evaluating the safety of essential oils. However, it must be borne in mind that it is the responsible person's obligation to implement the necessary means to ensure safety for consumers.

In accordance with guidelines for cosmetic products [27-30], an evaluation of essential oils by a safety assessor could include:

- an analytical phase in which the quantitative composition of the essential oil will be determined as exhaustively as possible, by the implementation of appropriately justified analytical methods;

- an extensive literature search concerning the essential oil and its chemical constituents identified during the analytical phase;
- a hazard characterisation of these chemical compounds individually and, when possible, of the mixture of the essential oil considered;
- an evaluation of exposure under use conditions (including but not limited to dermal exposure and by virtue of the volatile characteristics, inhalation);
- a risk assessment using all this information obtained.

If this data profile is insufficient to perform a risk assessment, it is possible to justify the use of means involving an *in silico* structure-activity research approach supplemented by toxicological studies. In all cases, the lack of available safety studies must be justified.

Hazard characterisation depending on available safety data of an essential oil may generally be related to one of the following approaches based, in order of priority, on the:

- available safety data;
- threshold of toxicological concern.

Many essential oils and their constituents have a high sensitising potential. Sensitisation can occur via dermal exposure or by inhalation. The SCCS's opinion on fragrance allergens in cosmetic products systematically and critically reviews the scientific literature to identify fragrance allergens, including natural extracts, relevant to consumers [6].

Risk assessment of a cosmetic product containing essential oils is based not only on the intrinsic hazard data but also on the exposure to the essential oils in question or their constituents. The exposure data will be defined on a case-by-case basis depending on the product's use. The following parameters should be taken into consideration:

- type of cosmetic product;
- concentration of the substance in the finished cosmetic product;
- amount of product used for each application;
- frequency, duration, area and site of application;
- target population;
- normal and reasonably foreseeable use conditions;
- area of exposure to the sun.

It is necessary to refer to the SCCS guidelines which indicate the average area per type of cosmetic product as well as the daily exposure to cosmetic products [28].

For the toxicological profile of essential oils, skin sensitisation is a crucial element. Some essential oils present a potential to cause skin sensitisation, which is a growing concern. The SCCS has reported the clinical evidence regarding sensitisation to essential oils in the opinion of 2011 [pages 53-57] [27].

The dose-response relationship between exposure to contact allergens and induction of allergy (i.e. sensitisation) is well established in animal models and by experiments in healthy volunteers. It seems that not only the dose per unit area of allergen, but also the number of exposures, i.e. the accumulated dose, is of importance for the risk of induction of contact allergy. The induction of contact allergy is an immunological process (type IV-allergy), which is without any clinical symptoms. In the case of continued exposure or re-exposure with a sufficient dose of allergen, elicitation will occur. Elicitation is an inflammatory response (eczema) with clinical symptoms of erythema, induration and in some cases vesicles. It was not possible to provide a safe threshold for natural extracts of concern, as no specific investigations exist and the model providing the general threshold (0.01 %) has been based on individual chemicals only. However the SCCS considers that the maximum use concentration applies to the identified chemicals both if added as chemicals or as an identified constituent of a natural ingredient. This will also reduce the risk of sensitisation and elicitation from natural extracts.

4.1. Approach based on available safety data

The intrinsic hazard characterisation and risk assessment under conditions of reasonably foreseen use require a sequential approach based first on literature data concerning the essential oil concerned and its chemical components. In the absence of data, toxicological studies must be used to identify and characterise the hazard of the essential oil. There is extensive discussion on this information in the SCCS guidance note [28]. Assessments must be compliant with the provisions of Regulation (EC) No. 1223/2009, as amended.

4.2. Approach based on the threshold of toxicological concern

The concept of the threshold of toxicological concern (TTC) may be used for chemically defined substances present at low concentrations and for which toxicological data is insufficient, but for which reliable exposure data is available. The TTC was developed to assess substances of unknown toxicity which are present as contaminants in food. It is a probability-based screening tool and TTC values are derived from theoretical databases that are based on systemic effects after oral exposure. The concept relates only to systemic but not local effects. Thus, allergy, hypersensitivity and intolerance – toxicological endpoints of concern with regard to essential oils – are not taken into account. Additionally, if this concept is used in the field of cosmetic products, appropriate methodologies need to be developed to allow for route-to-route extrapolation from oral to dermal exposure. It should be noted that the TTC approach differs from other alternative approaches because it focuses more on risk assessment (i.e. the establishment of a permissible exposure limit) than just on the hazard characterisation. In the case of essential oils, the TTC approach could be applied to chemically identified constituents present in small amounts and for which the toxicological data is insufficient. Attention is drawn to the SCCS, SCHER and SCENIHR joint opinion on Use of the Threshold of Toxicological Concern Approach for Human

Safety Assessment of Chemical Substances with focus on Cosmetics and Consumer Products [28].

4.3. Finalisation of risk assessment

Based on the data (hazard and exposure) examined by a safety assessor, the conclusion of the expert report must answer the following questions:

- Can the essential oil be used in the cosmetic product to be considered safe for the consumer?
- Is the essential oil subject to restrictive conditions of use in the cosmetic product?
- Does the essential oil require special conditions of use in the cosmetic product?

It is understood that the assessment of risk for humans of a finished cosmetic product remains the responsibility of the safety assessor; this includes if the cosmetic product contains essential oils. Elements and procedures used for risk assessment must be explicitly described and the reasoning that led to the conclusion must be clearly justified.

5. Conclusion

This document is intended for operators in the cosmetics industry who have a responsibility to ensure the safety of cosmetic products. That includes, but is not limited to, responsible persons who manufacture, contract the manufacture or import cosmetic products containing essential oils. It aims to highlight the importance of the quality of essential oils and of the starting materials from which they are obtained and also to provide recommendations on the risk assessment of essential oils and the potential implications when including them in cosmetic products.

Essential oils have been used for centuries in cosmetic products. This history of use can be a reassuring factor to be taken into account. However, some of these oils may be harmful to consumers when added to cosmetic products due to their transdermal absorption or inhalation. The scientific publications available are often limited and only describe the toxicology of one or other of the pure constituents present in an essential oil and do not specifically describe the use of these essential oils in cosmetic products. There is a paucity of reliable clinical toxicological work in this area.

Although essential oils are generally used in a diluted form in cosmetic products, this is not always the case. If products containing high concentrations of essential oils are misused the effects can be harmful especially in sensitive people, such as sensitised individuals and children. In addition to this, essential oils can have variability parameters which can significantly alter their chemical profile and therefore increase the risk of toxicity. This in turn could influence the quality and safety of the finished cosmetic product. It is therefore important to ensure that defined quality factors exist for essential oils and are considered by all operators when placing such cosmetic products on the market.

6. Acknowledgements

The first edition of the present guidelines on the use of essential oils in cosmetic products was prepared by Ms Sinead Hickey and Dr Darren Scully of the Health Products Regulatory Authority, Ireland).

Great appreciation is due to Ms Sinead Hickey and Dr Darren Scully for their hard work and dedication to the subjects covered.

Our special thanks go to Ms Cécile Verdier (ANSM, France) and Robert Anton (France), Professor emeritus of the University of Strasbourg, who initiated the elaboration of European guidelines based on national recommendations in the field.

Substantial contributions to the work were made by Ms Dominique de Clock (SPF, Belgium), Dr Annegret Blume (BfR, Germany), Dr Anke Meisner (BMEL, Germany), Mr Durk Schakel (NVWA, Netherlands), Ms Ngoc-Hang Huynh (MPA, Sweden) and Ms Carole Meylin-Gonin (FVO, Switzerland).

We thank all the national experts who supported the preparation of these guidelines with their constructive comments.

Release of the guidelines was approved by the Consumer Health Protection Committee of the Council of Europe (list of national representatives provided in the Annex).

For the Secretariat, drafting and editing was co-ordinated by Ms Susanne Bahrke, Ms Amela Saračević and Mr David Crowe.

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