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Product Information File and Safety Assessment: Legislative Requirements, Practical Implementation of Construction and Maintenance

1. Purpose of the Product Information File

The new EU Cosmetics Directive 1223/2009 requires the product information file (PIF) for each cosmetic product sold in the European Union for reasons of effective market surveillance. As a result, consumer protection is also paramount in the requirement for the creation of the PIF. This and more is once again clearly expressed in point 61 of the preamble:
»*In order to ensure effective in-market control, a high degree of administrative cooperation amongst the competent authorities is necessary. This concerns in particular mutual assistance in the verification of product information files located in another Member State*«.

1.1 Requirements of the Product Information File

According to EC regulation 1223/2009 for cosmetic products, point 17 of the preamble, the product information file must

- be available to a Member State: »*For the purpose of effective market surveillance, a product information file should be made readily accessible, at one single address within the Community, to the competent authority of the Member State where the file is located*«.

This is further defined in Chapter III, »Safety assessment, Product Information File, Notification«, Article 11 § 3

- be easily accessible: »*The responsible person shall make the product information file readily accessible in electronic or other format at his address indicated on the label to the competent authority of the Member State in which the file is kept*«.

- Be written in an international language: »*The information contained in the product information file shall be available in a language which can be easily understood by the competent authorities of the Member State*«.

The product labelling in accordance with Chapter VI of »Information for consumers«, Article 19 »Labelling«, § 1 contains the following important information for the EU authorities to facilitate cooperation:

- Defining the location where the product information file is kept with the following information: »*[...] the name or registered name and the address of the responsible person. Such information may be abbreviated in so far as the abbreviation makes it possible to identify that person and his address. If several addresses are indicated, the one where the responsible person makes readily available the product information file shall be highlighted. The country of origin shall be specified for imported cosmetic products*«.

1.2 Definition or responsibilities

It is described in Chapter 1.1 that the cosmetic product's labelling must be such that the person responsible for the availability of the PIF is recognisable.

1.3 Requirements for Maintaining the Availability of the Product Information File

Under Chapter IX of the EC Regulation 1223/2009 on cosmetic products »Administrative Cooperation«, the PIF is checked only at the particular place where this is kept – with appropriate labelling as mentioned above. The respective local authorities, which are required to conduct an audit, must contact the competent local authority. Nothing has changed in the approach here.
For purposes of effective market surveillance and consumer protection, see also Article 30: »Cooperation regarding verification of product information files« serves as a review, »*whether the product information file satisfies the requirements referred to in Article 11(2) and whether the information set out therein provides evidence of the safety of the cosmetic product*«.
Furthermore, the legislation states that »*The requesting competent authority shall provide a motivation for the request*«. This means it is important to remember that this only applies to the reasonable suspicion of a safety risk. Even if the requisite due diligence is always at the forefront of a responsible business, it needs to be explicitly pointed out that it may be legitimate to question the official request of other Member States and not allow yourself to be put under pressure. Experience shows that some sales partners would like to know as quickly as possible about requests made by the competent authorities. This often occurs because of ignorance or bad experiences from the past with regard to behaviour of authorities such as in the former East-

ern Bloc countries. The competent authority shall immediately arrange for the review and inform the requesting authority of its findings.
It is also important that it is stated in the text of the law that the PIF should be made available to the competent authority in a language which is easy to understand. English has meanwhile gained a high penetration rate within the EU, so it can be assumed that the creation of the PIF in English as the sole foreign language should be widely accepted and additional translation work into other potential EU languages is not necessary.

2. Changes in the New EC Cosmetics Directive

The question now arises as to the changes which have occurred with the implementation of the new EU Cosmetics Directive with regard to the creation of the product information file and how these can be implemented and become reproducible within a reasonable time frame, particularly in smaller companies. Why particular attention should be paid to this point pertains, on the one hand, to the required content of the PIF and also, on the other hand, to the new notification procedure. In fact, necessary components of this future reporting procedure are also included in the PIF.
In addition, it is important to note that the PIF is naturally subject to continuous updates and must be retained for a period of 10 years after the last batch has been released. The prescribed period is explicitly defined in Chapter III, »Safety assessment, product information file, notification« Article 11 »Product information file« § 1.

2.1 Composition of the Product Information File

The definition of the PIF's contents should be viewed in the context of consumer protection as should the intent of the statutory requirements.
According to Article 11, Paragraph 2 of the EU Regulation 1223/2009 on cosmetic products, the following content is required:

a) »*The product information file shall contain the following information and data which shall be updated as necessary*«.

b) [...] *Safety assessment*.

c) »*Description of the method of manufacturing and a statement on compliance with [...] good manufacturing practice*«.

d) »*Where justified by the nature or the effect of the cosmetic product, proof of the effect claimed for the cosmetic product*«

→ Dermatological tests or
→ clinical tests
→ literature references.

e) »*Data on any animal testing performed by the manufacturer, his agents or suppliers, relating to the development or safety assessment of the cosmetic product or its ingredients, including any animal testing performed to meet the legislative or regulatory requirements of third countries*«.

If you look at the required content, one could say regarding point a.) that it deals with the »character« of a product with composition, production method, filling requirement, specification, printing materials, etc. The documents should be so extensive here that the product is clearly assigned to the PIF, that is similar to a bill of materials for the manufacture of the cosmetic item. The production method together with the declaration on compliance with GMP has been managed in the product dossier.
Point b) Safety assessment, for details see section 2.2)
Point c) Statement of compliance with the GMP (special instructions for non-EU suppliers, see section 2.3)
Point d) requires the evidence for advertised statements as to the effects of the product in question. It certainly makes sense to file product-specific dermatological tests here, for example, in addition to the compatibility test (also called »patch test«) and efficacy testing, if required. Of course, literature references can also be filed here, and documents relating to the ingredients used should be documented in the raw material records to facilitate the development of these active ingredients for future projects.
In practical terms, the data referred to in point e) required from animal tests performed in connection with the development or safety assessment of the cosmetic product refer to its raw material specifications or toxicological characteristics. Depending on the number of operating resources, the question arises as to whether a simultaneous update of raw material specification in the PIF of the respective products for which the raw material in question is used is even feasible or not. Perhaps it makes sense to file relevant entries relating to one's own information or supplier agreements here and to refer to the specific raw material specifications.

2.2 Required Information for the Safety Assessment

To ensure the safety of the cosmetic product, as required by Article 3 of the EU Cosmetics Directive 1223/2009, the product will undergo a safety assessment in its entirety and a safety assessment report is created. The requirements for the safety assessment report as well as the safety assessment are reproduced in Annex I, Part A and B. These requirements are based on the documents and information which are needed for the product information file. It is established in a binding manner in the EU Cosmetics Regulation 1223/2009 for the first time, which data and information should be present as the basis for assessment and must be taken into account.

2.2.1. Annex I, Part A: Cosmetic Product Safety Information

Quantitative and Qualitative Composition of the Cosmetic Product

The qualitative and quantitative composition of the cosmetic product, including chemical identity of the substances (incl. chemical name, INCI, CAS, EINECS/ ELINCS, where possible) and their intended function. Particular attention should be paid to the following points:

Stating the name of the raw material: Complete raw material names should be provided here. There should be no simplified use of the name; for example, in the case of plant extracts it is essential that the extract concentration and extraction agent is known.
By providing the material composition of the raw materials, care should be taken to ensure that substances for preservation or stabilization (such as antioxidants) are also listed.
Stating the CAS or EINECS/ELINCS number: The information from the supplier's records must be examined here. The INCI as well as the CAS or EINECS/ELINCS number are often not updated.
Concrete, percentage content information: The formulation is protected by confidentiality agreements, of course.

Physical/Chemical Properties and Stability of the Cosmetic Product

Knowledge of the properties as well as the substances and mixtures used and the resulting product will be required here. The basic characteristics and functions of the substances and mixtures used can be found in the safety data sheet, technical data sheet, specifications and certificate of analysis of the raw materials extracted. However, the specification of the cosmetic product is of concern.
The product stability »under reasonably foreseeable storage conditions« refers to the durability of the product while being stored by the customer. A review of the final packaging is essential, as it affects the properties of the storage stability. For this there are tests at various temperatures and temperature gradients, humidity, and also with and without exposure to light. The product stability under storage conditions can be viewed as closely associated with the microbiological quality of the product. Cosmetic products may be exposed to not only microbial spoilage changes during storage and thus present a hazard.

Microbiological Quality

The microbiological quality of both raw materials and the product should be taken into account here.
Preservation stress tests do not provide reliable values for every product form (such as soaps, water-free products, o/w emulsions) and are therefore not always regarded as feasible. Reputable testing laboratories are here to advise you.
To increase the protection of vulnerable groups of consumers, it is advisable to review the microbiological quality under particularly stringent criteria for »*cosmetics used around the eyes, on mucous membranes in general, on damaged skin, on children under three years of age, on elderly people and persons showing compromised immune responses*«.

Impurities, traces, information about the packaging material

Impurities and traces from the raw materials can be diversified in nature. Depending on the raw material in question, these may be residual solvent, residual basic materials such as monomers, by-products, heavy metals, pesticides or PAHs. This is not meant to be an exhaustive list of all possible traces or impurities. Each raw ingredient is to be checked separately for the possibility of impurities and traces.
The inadvertent presence of traces of banned substances can possibly be tolerated, provided that it can be demonstrated that this is technically unavoidable and that the final product is safe. By comparing the qualities of the raw materials available on the market (»benchmarking«) it can be seen which levels of cleanliness are technically possible and therefore that traces or residual contents are regarded as technically unavoidable. With regard to the relevant characteristics of packaging material, purity and stability in particular, material specifications may already provide the necessary information. If the packaging material for food and pharmaceutical products is suitable and approved, analogies can be drawn for cosmetic products. Documents can be displayed here from the supplier, that the packaging material complies with Regulation (EC) 1935/2004 (European Commodities Regulation) [4] or Directive 2002/72/EC [5], for example. As with food or pharmaceutical products, when it comes to the choice of packaging material, the matrix of the cosmetic product should be considered (such as o/w, w/o) as well as any possible adverse effects from the product packaging. In the event of, for example, exposure to light, gas permeability, migration (of the packaging material's ingredients or the outer imprint into the cosmetic product) and adsorption (of cosmetic ingredients on the packaging material), changes to the packaging material and the cosmetic product itself may be caused here.

Normal and Reasonably Foreseeable Use

It is anticipated, for example, that some portion of lipstick or toothpaste is swallowed (especially by children). However, it can be assumed that a product for facial care is not used for the entire body, and has a plausible prescribed use for individual body parts (such as neck and décolleté, as well as additional hands and forearms). This can be seen in many products simply by the amount of product offered.

Exposure to Cosmetic Products

These in turn include several parameters:

a) Location(s) of application: in the context of the normal and reasonably foreseeable use, there is increased focus on particularly sensitive areas such as mucous membranes or infant skin. In addition, the presentation of the product must be considered (with application instructions and warnings, for example).

b) Application surface(s): the determination of the surface is closely linked to the location(s) of application. The surface can be determined using average values. Also included here is reasonably foreseeable use, such as the application of face cream on neck and décolleté.

c) Amount of product applied: the amount of product is also connected to location and surface of the application. Some products can be applied several times a day (lipstick, soap, toothpaste, etc.), some products very generously, others more sparingly. The COLIPA has conducted exposure studies for the application of cosmetic products in Europe and elicited average use levels.

d) Duration and frequency of use: in addition to the values from exposure studies for application recommendations on the packaging - if present - they can fall back on their own experience here.

e) Normal and reasonably foreseeable exposure: »normal and reasonably foreseeable use« points are considered here.

f) Target groups (or exposed groups). The possible exposure of a specific group of people should also be considered: Depending on the target group, the cosmetic product must take particular features of the skin texture into account. Target groups can be infants and young children, pregnant women, men (shaving products), for example.

g) If necessary, when considering the exposure, the particle size of raw materials or the application of additional products should be considered. Therefore, raw materials in the nanoscale range have different properties than larger particles, for example. It should, however, be specifically checked whether it deals with soluble, biologically unstable (such as nano-emulsions) or insoluble, biologically resistant substances. It can further be estimated from exposure to sprays based on the particle or droplet size, how deep the cosmetic product penetrates the mouth, throat and lungs and if it can potentially cause adverse effects.

Exposure to the Substances

The exposure to the ingredients can be determined from the information on exposure to the cosmetic product and the contents of each substance. The relevant toxicological endpoints are included here.

Toxicological Profiles of Substances

As relevant toxicological endpoints, local toxicity (skin and mucous membrane irritation), sensitisation of the skin and phototoxicity (for UV-absorption) have particular influence on the assessment. Furthermore, the relevant toxicological path of absorption and systemic effects are taken into account. Based on NOAEL (no observed adverse effect level), the MoS (margin of safety) is calculated. For calculation of the necessary NOAEL values, not every substance from raw material suppliers is delivered. Nor are any raw material NOAEL values determined. The calculation of MoS can be waived if it can be properly justified. If, for example, an absorption or systemic availability due to skin penetration data, molecular size and octanol-water partition coefficient, can be ruled out, or if a recognised scientific body has established safe levels of the substance in comparable products (e.g. SCCS, CIR (Cosmetic Ingredient Review)), this can be used as justification.

The assessment can also be influenced by the considerations of the influence of particle size, impurities of the used (raw) materials and interactions of the ingredients of the cosmetic product.

Provided that for assessment analogies are drawn to assess a particular substance, for example, where there are only data for substances of the same substance group, then this data has to be proved and justified.

Of course, all information sources are clearly marked.

Adverse Effects and Serious Adverse Effects

All information on adverse and serious adverse effects should be recorded and evaluated here, in the form of statistical data, for example.

Undesirable effects are according to definition (Article 2, Letter o) an adverse reaction for human health attributable to the normal or reasonably foreseeable use of a cosmetic product. Serious undesirable effects (Article 2, Letter p) results in temporary or permanent functional incapacity, dis ability, hospitalisation, congenital anomalies or an immediate vital risk or death.

Information about adverse and serious adverse effects of the product itself should be placed in the safety assessment at the first sign of risk, since they were not yet available up until this point. Experience with similar products may, however, assist in an assessment. As soon as adverse effects are known, then it is necessary to consider a product revision. It is a moot point whether a product which causes serious adverse effects should remain in the market in its current composition.

Information About the Cosmetic Product

Among the relevant information required here are included dermatological studies (such as patch testing and application testing), efficacy studies (such as for sun protection products) but also information about used (raw) materials from publications.

2.3 Notes on GMP Requirements for Non-EU Suppliers

According to Article 1 and Article 8 of the Cosmetics Regulation 1223/2009 (1), the manufacture of cosmetic products must be done in accordance with good manufacturing practice to ensure a high level of health protection.

In the EU Official Journal, the standard »ISO 22716 - Guidelines for Good Manufacturing Practice (Cosmetics GMP)« was published (2).

This standard must be followed. The authorities within the European Union consider this standard as the basis for site inspections.

The Cosmetics Regulation, however, does not necessarily require ISO 22716 to be reviewed by an external company. A document issued by the manufacturing company itself is sufficient for it to be included in the PIF.

Since the responsible person, when importing cosmetic products into the European Union, is often unaware of the actual source of the products, and as a result is not familiar with the manufacturing company in a third country, the submission of just the aforementioned document can present a risk. In case of defective production quality, the distributing company is fully responsible in the EU. An emergency as well as an endangerment of health may be construed as gross negligence if the distributor has not provided information in any way as to »production quality«. An external study by a consultant or specialist institution has a fundamental advantage here, as

the European point of view or interpretation of ISO 22716 will also be used in their investigations (3).

3. Documentation Comparison

It was pointed out already that the PIF must be continually updated and must be retained for a period of 10 years after distribution of the last batch of each cosmetic product. If one compares the documents required for the PIF with those for the safety assessment and the necessary notification procedure, it is noticeable that some of them must be created for all three documentation requirements

4. Challenge: Implementation in Practice

So if one takes a look at a comparison of the various documents necessary, it becomes clear that it will be difficult to keep track of all updates to be made, i.e., which documents should be amended, where to file these, what are the effects of an update process? Should the updated documentation only be stored (such as changes to the production method, for example)? If so, where does the storage need to take place (answer: PIF and possibly safety assessment). Or for more severe changes, such as, for example, a formulation change which has an impact on the toxicological profile data and, at the same time, results in a new report of the notification procedure.
With a manageable range of products, that may still work by filing as a hard copy in various files. However, consideration should continue to be given to how best to assess the personnel requirements needed. Each employee must also be able to demonstrate they have the skills required for filing in order to evaluate the revised documents. I.e., cross-checking the documentation is always useful and saves a lot of tedious correction of work, if, for example, in the creation of the safety assessment, incorrect data is entered or responding to enquiries for the reporting process is required.
It will be necessary to consider how to proceed if

1. the safety assessment is prepared by external service providers
   or
2. the cosmetic product is procured externally.

In the first case, the external service provider must make many documents available electronically and that can mean a large data flow. The safety assessment with all this data must again be stored in the PIF. The implication for the responsible employee is that the overview is observed and extreme caution is used in the care of the documents, with the necessary expertise and an overview of the entire range.
Regarding Point 2, it must be conducted in such a way – as already mentioned – that clear arrangements are made with the suppliers, to ensure that the client is truly notified of any change.
A closer examination of these requirements will reveal without question that the work can be expected to amount to a document library very quickly with the storage and updating of all required data. As an estimate, it is useful to calculate how high the number is of existing products in the company, annual changes in formulations and new product introductions, product redesigns (such as changes to the artwork without any alteration to the formulation). It is also important to note how quickly suppliers respond to product changes and how much effort is required for possible collaboration with external service providers in order to produce the safety assessment.
When working with external service providers, a convenient way to access the document library would be to make it available to the service providers using a password. One can thus avoid the time-consuming email traffic. It is often possible for an automatic notification to be sent to the participants whenever changes are made in the document library so that the human factor of forgetting is avoided. Practically, this means that a modified formulation for an item is stored and the activated service provider automatically gets a message that an update to the safety assessment is instructed. The service provider accesses the modified formulation with all the necessary raw materials. The raw material documents should also sensibly be maintained in the document library as a resource file. He or she then creates the revised safety assessment and then loads it back into the document library.
The versioning/archiving can be easily take place in a document library. If one takes into consideration the amount of paperwork that can accumulate over time with a storage period of 10 years, it obviously makes sense to think seriously about electronic data storage.
It is desirable for the future that service providers come up with a solution for their customers here, since small businesses already have to calculate their personnel requirements very closely, especially when there is a lack of both personnel with the appropriate expertise who can be used solely for documentation maintenance and available staff who can deal with their own creation and maintenance of required software.

References

(1) EU Cosmetics Regulation 1223/2009

(2) DIN EN ISO 22716Leitfaden zur guten Herstellungspraxis (Kosmetik-GMP)

(3) Cosmetic Campus Fachbuch »EG-Kosmetikverordnung 1223/2009«

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