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Cosmetovigilance: definition, regulation and use "in practice"

Cosmetovigilance is a recent concept. The term itself has just been indexed. It is a form of health public surveillance with a public health objective; it therefore differs from the surveillance carried out by industrialists, who aim at the safety of the product for commercial purposes, and differs from peer surveillance (Revidal-Gerda), whose purpose is medical. Cosmetovigilance concerns cosmetic products. The 2006 European resolution has laid the ground work for a cosmetovigilance system based on case notifications. As of 2013, the new European regulation requires that serious undesirable effects reported to the competent authority should be transmitted to the competent authorities of the other Member States and to the person responsible for the cosmetic product. Two problems are yet to be solved: causality assessment and reporting categories. Cosmetovigilance systems are genuine means of obtaining information on the safety of cosmetic products and their ingredients. They can be used by Europe to check that new directives ensure a high level of safety. Cosmetovigilance makes it possible to rule out or control potentially hazardous ingredients and can thus set our minds at ease about the products placed on the market.

Key words: cosmetic adverse effects, cosmetovigilance, peer surveillance, European regulation, PPD, causality assessment

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When it was first used in the French literature in 1997, the term "cosmetovigilance" was not indexed on an international scale [1]; the concept could be translated by "surveillance" or "monitoring cosmetic product safety". Before addressing this fairly recent subject, it seems necessary to specify what surveillance is and what cosmetics are.

Cosmetovigilance is a form of health surveillance *(table 1),* i.e. public surveillance with a public health objective. It thus differs from the surveillance carried out by the industry, whose aim is the safety of the product for commercial purposes, and differs from peer surveillance (Revidal-Gerda) whose purpose is medical [2]. The scope of cosmetovigilance is cosmetic products.

Table 1. Definition of health surveillance

- Collection and identification
  - of adverse effects on man
  - directly related or not
  - to the use of a technique, a treatment or a product
- Analysing the data collected
  - causality
  - frequency
  - severity
- To propose remedial action or preventive measures
- Public Health Objectives:
  - improving knowledge, epidemiology
  - monitoring and alerting
  - risk management

Cosmetics are products which meet the definition given in Directive 93/35 [3]: "A "cosmetic product" shall mean any substance or preparation intended to be placed in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and/or correcting body odours and/or protecting them or keeping them in good condition". Cosmetic products must also comply with the annexes[1] and marketing regulations. They were regulated by directive 76/768/EEC [4], which was replaced in July 2013 by the European regulation on cosmetic products [5]. Cosmetic products are defined according to their function and site(s) of application. They can be used at home but also at work, both as hygiene or occupational products. The restrictions on the use of some ingredients in the annexes mean that any ingredient not on the list is allowed. Thus, as the industry is quite creative and is always

[1] Annexes are mainly lists of substances established to ensure the safety of cosmetic products. There are VIII annexes. The major ones are: annex II, which concerns banned ingredients, and annex III, which provides a list of the substances subject to restrictions or specific conditions of use. Annexes IV, VI and VII are restrictive lists of allowed colouring agents, preservatives and UV filters.

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looking to improve its products, it is constantly using new ingredients not listed in the annexes. Such ingredients are new potential allergens. Unlike drugs, there is no agency to assess the safety of cosmetic products, no marketing authorisation with specific requirements, no evaluation of the risk-benefit ratio and no guarantee of constancy from one batch to another. Cosmetics cannot claim therapeutic benefits and, in addition, they "must not cause damage to human health when applied under normal or reasonably foreseeable conditions of use" 93/35/EEC [3]. Despite this statutory obligation not to cause damage to human health when applied under normal conditions of use, past studies in the general population showed that about 12% of users had experienced undesirable effects with one or several cosmetic products in the preceding five years [6].

The early days of cosmetovigilance in France [7]: The Public Health Law of August 2004

Although a study on the usefulness of implementing a cosmetovigilance system carried out in Sweden between 1989 and 1994 received a small number of adverse effect notifications and thus concluded that cosmetovigilance was of little interest [8], and because, within the European Union, the states are responsible for the safety of products, France decided to determine whether monitoring cosmetic products was of interest to public health. Thus, in 1999 the government decided to replace the Medical Drug Agency by AFSSAPS[2]. It entered agreements with the French national authority for health (HAS) when the latter was created in 2004 and which is now being replaced by the French National Agency of Medicine and Health Products (ANSM) [9]. Within AFSSAPS, the cosmetology commission was created in 2000 and the Working Group on the Safety of Use of Cosmetic Products (GTSPC) was established in 2002. The mission of this working group was to set out the basis of a surveillance system, of a national cosmetovigilance system and to provide the Director General with advice on the organisation of data collection on adverse effects in cosmetology. It should be noted that, since 1996, Revidal-Gerda, a peer surveillance network, had been engaged in active cosmetovigilance with data centralised by Dr A. Pons Guiraud [10]. In 2004, GTSPC launched a pilot study that invited practitioners and companies to report undesirable effects observed over a 4-month period. This study resulted in the Public Health Law of August 2004 that laid the groundwork for cosmetovigilance in France [7] *(table 2)*. This law defines what a serious undesirable effect is. Although very few life-threatening cases involving cosmetic products have been reported [11, 12], cases of cosmetic-induced sensitisation in patients who must then strictly avoid exposure to an allergen/ingredient, as well as cases of permanent incapacity to work when the product is indispensable for work (i.e. hair dyes for hairdressers or acrylates for nail technicians), are not uncommon. The 2004 Public Health Law stated that adverse effects from misuse were to be reported since, if repeated misuse occurs, it may be due to inappropriate packaging or ambiguous communication about the product. All health care professionals were bound by the mandatory reporting of serious undesirable effects. In addition, any health care professional could also notify any seemingly serious undesirable effect. For example, contact urticaria induced by a cosmetic product can be deemed serious by the practitioner, even if the lesions are temporary, as it may be an IgE-mediated reaction and may lead to anaphylaxis [13, 14]. As such, the practitioner can report it to cosmetovigilance. This system based on the reports by health care professionals is complemented by the obligation for companies to declare serious undesirable events notified to them to the General Directorate Competition, Consumers Affairs and Fraud Control (DGCCRF) and to keep epidemiological data available for AFSSAPS.

The results of French cosmetovigilance can be found on the ANSM website. This surveillance has made possible the detection of emerging allergen ingredients such as vitamin K[3], which caused sensitisation when it was used as an ingredient in cosmetic products [15]. The use of vitamin K in cosmetics was prohibited as a health protection measure. Cosmetovigilance has led to a greater awareness of the risk of paraphenylendiamine (PPD) sensitisation from temporary black tattoos. In France, sustained media campaigns have reduced this risk and cosmetovigilance has clarified the non-exclusive role of sensitisation to PPD in hair dyes from temporary black tattoos, as a certain number of reported reactions to hair dyes from PPD sensitisation concerned users who had never had such temporary black tattoos [16]. Thus French cosmetovigilance was able to contribute to the new regulation on hair dyes. This system also detected sensitisation to octocrylene due to photosensitisation from ketoprofen gel [17]. The number of reported cases barely reaches 200 per year, which seems relatively low when considering the more than 10,000 cases reported annually by medical device vigilance systems. However, the two systems cannot be compared as there is a wide range of medical devices. Such devices, when they have a therapeutic claim, have a risk-benefit ratio that is assessed by a notified body before they are put on the market. Besides, it is known that their safety level is being questioned in Europe.

Implementing a cosmetovigilance system in Europe [18] Council of Europe Resolution ResAp (2006)

European consultations have shown that medical practices, the way member states are organised, and health care access for patients greatly differ from one country to another. In some European countries, the European Society of Contact Dermatitis (ESCD) developed efficient computer systems

[2] French Health Products Safety Agency

[3] Vitamin K was allowed in cosmetic products as it was not listed in the annexes. The enquiry was prompted by the many cases of sensitisation reported to cosmetovigilance and revealed that this ingredient, because of its structure, was highly reactive when applied on the skin.

Table 2. Text on cosmetovigilance in the 2004 Public Health Law.

For the purposes of this article, serious undesirable effect means a harmful and unintended reaction occurring in normal or reasonably foreseeable conditions of use of a cosmetic product in humans or resulting from misuse which either would require hospital treatment or result in permanent or temporary functional impairment, disability, immediate threat to life, death or congenital defect or malformation.
To implement the cosmetovigilance system, any health care professional who notices a serious undesirable effect likely to be induced by a cosmetic product referred to in article L.5131-1 must notify it without delay to the Director General of the French Health Products Safety Agency.
In addition, the health care professional reports undesirable effects which, although they do not meet the abovementioned definition, he or she deems particularly serious and that thus warrant such a notification.
In his or her notification, the health care professional shall specify if the undesirable effect results from a misuse.

to process contact dermatitis test results [19]. Cosmetovigilance could have been based on the analysis of those results. However, European consultations have shown that the ingredients in cosmetic products are seldom specific; indeed, preservatives, perfumes and para-derivatives can also be found in detergents, industrial products, food and so on... Thus, an increase in the number of positive test results to PPD or to eugenol in a database is not necessarily due to sensitisation from cosmetic products. Besides, a certain number of undesirable effects cannot be considered as delayed sensitisation, thus convulsions or anaphylaxis-type reactions are not recorded in databases on contact dermatitis. The 2006 European resolution laid the ground-work for a cosmetovigilance system based on case notifications [18]. In this resolution, the European Council recommends that each of its member states should implement a system to record the undesirable effects of cosmetic products with a view to protecting human health. Following this resolution, cosmetovigilance systems were created in Belgium, Norway, Sweden, Denmark, Germany and Italy [20-23]. They all collect cases reported by health care professionals. Although the quality of the cases is good, their number remains quite small. A pilot study is worth mentioning: the Dutch public authorities launched a pilot study in order to list the undesirable effects of cosmetic products and to identify the ingredients involved [24]. Cases were reported by volunteer general practitioners and dermatologists who carried out patch-tests and consumers had access to a notification website. In addition, public campaigns in the mass media encouraged consumers to report undesirable effects. Between July 2009 and May 2011, over 1,600 undesirable effects were reported. The number of consumer notifications increased after each media awareness campaign. In 1% to 4% of cases, the undesirable effects were considered serious. The most frequently reported cosmetic products were make-up, moisturisers, hair care products and soaps. The most frequently identified allergens were isothiazolinones and fragrance ingredients, although perfumes as such were not involved. A new allergen has "emerged", namely co-polymers/cross-polymers. The main locations were the eyelids and the face and neck; as for cases reported by dermatologists, the hands were more frequently affected than the neck. This was the first study to test the possibility of collecting consumer notifications. It seems that consumers are qualified to report undesirable effects, all the more so as media campaigns enhance their awareness of the possibility of reporting such effects. The results of this pilot study are comparable to what Revidal-Gerda and the French cosmetovigilance system have observed, since 1996 [2] and 2004, respectively. Cosmetovigilance is an excellent way of assessing the safety of cosmetic products, of detecting hazardous ingredients and of witnessing the emergence of new allergens. In 2012, the Netherlands Food and Consumer Product Safety Authority and the Ministry of health decided to continue to register undesirable effects and were willing to work towards establishing a European cosmetovigilance network.

The future of cosmetovigilance [5] EU Regulation 1223/2009

In 2013, the new European regulations came into effect. Articles 22 and 23 require member states to provide surveillance authorities with the necessary powers, to monitor their functioning every four years and to make these results available to the public. These articles require that serious undesirable effects reported to the competent authority should be transmitted to the competent authorities of the other Member States and to the person responsible for the cosmetic product. Serious undesirable effects shall be reported by this person or by the distributor of the product; they can also be reported by health care professionals or even users. The undesirable effects that should be reported must occur under normal or reasonably foreseeable conditions of use.

Problems yet to be solved

Causality assessment [25]

The definition of causality assessment is slightly different for AFSSAPS and Colipa:

– For AFSSAPS, causality "assesses **the cause and effect relationship** between a cosmetic product and a specific clinical and/or paraclinical manifestation" (2010). Causality must be established for each product individually [9].
– For Colipa[4] "Causality assessment is particularly useful when the same product is involved in the occurrence of several cases of undesirable effects, when it makes it possible to determine the extent of a link of cause and effect between the cosmetic product and the undesirable effects observed and then to take these effects into account in the subsequent drawing-up of corrective measures such

[4] Colipa : European Cosmetic, Toiletry and Perfumery association

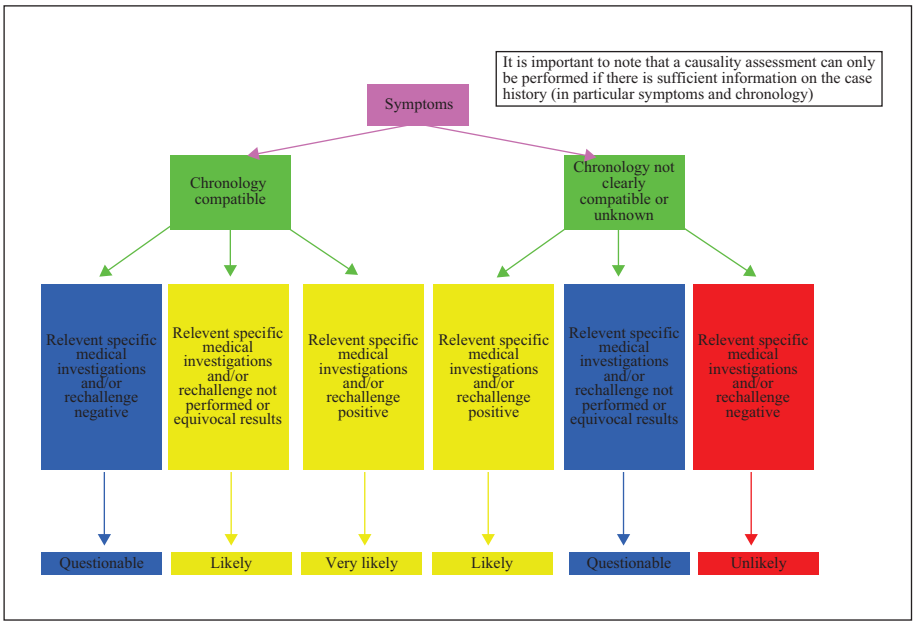


Figure 1. Causality assessment according to Colipa.

as investigations, recommendations on the proper use of the product, or regulations at national or European level (restrictions on use, warnings on packaging labels, limited concentration or prohibition).

– Several methods have been published. They are based on the analysis of evolving chronological and semiological elements. The results of relevant tests or of re-challenge tests can alter causality, for instance as regards contact allergy; appropriate patch testing provides a certain degree of causality. The AFSSAPS method is based on 6 criteria, divided into two groups, which are used to calculate a **chronological** score and a **semiological** score. The level of causality is determined using a decision table in which the scores are combined. The method has five levels of causality assessment: very likely, likely, not clearly attributable, unlikely and excluded. The causality assessment method by Colipa is based on three major criteria: symptomatology, chronology and results of specific tests. This method offers 3 levels of causality on the basis of a decision tree in which these criteria are combined: questionable, likely and very likely *(figure 1)*. Another method uses a flow chart as soon as the case has been reported, following a PLM (product lifecycle management) call approach. It is also based on chronological and semiological criteria and all the notifications can be analysed using 6 levels: irrelevant, not enough information, unlikely, possible, probable and certain *(figure 2)*.

Reporting category

According to the latest European regulation, the person responsible for the cosmetic product he put on the market shall report undesirable effects to the competent national authorities of the state in which they occurred. In France, according to the 2004 Public Health Law, health care professionals shall report serious undesirable effects as well as those they deem serious to the French National Agency of Medicine and Health Products (ANSM). It could be valuable and relevant for consumers to have an opportunity to report undesirable effects [24].

How do health care professionals use cosmetovigilance in practice?

Case notification

Since the 2004 Public Health Law, any health professional in France shall report serious undesirable effects – or those he deems serious *(table 2)* – connected to the use of cosmetic products, whether they are from misuse or not. The mission of the cosmetovigilance investigation will then be to assess case causality. In Germany, Belgium, the Netherlands, Italy and Portugal, cosmetovigilance is available to all health care professionals, although reporting to cosmetovigilance is not mandatory. The notification can be made on a sheet of plain paper or using the notification form *(figure 3)* that can be downloaded from the websites of the competent authorities: ANSM in France[5], the Ministry of Health in Belgium[6]... The following information should be mentioned: 1/ name of the reporter, 2/ name of the user affected by the undesirable effect (first three letters of the surname, first name, gender and date of birth), 3/ name of the cosmetic product concerned (full name, brand, use and, when possible, batch number). The product must be kept for further potential analyses. The undesirable effect must be described providing detailed chronological and semiolog-

[5] fax: 0155874260, mail : cosmetovigilance@ansm.sante.fr or by post at: Direction des Dispositifs médicaux thérapeutiques et des cosmétiques 143-147 boulevard A France 93285 Saint Denis Cedex

[6] fax: 02/524.73.99, mail : cosmetovig@health.fgov.be or by post at: Direction générale Animaux, Végétaux et Alimentation. Eurostation, bloc II, 7e étage, Place Victor Horta 40, boîte 10 B-1060 Bruxelles

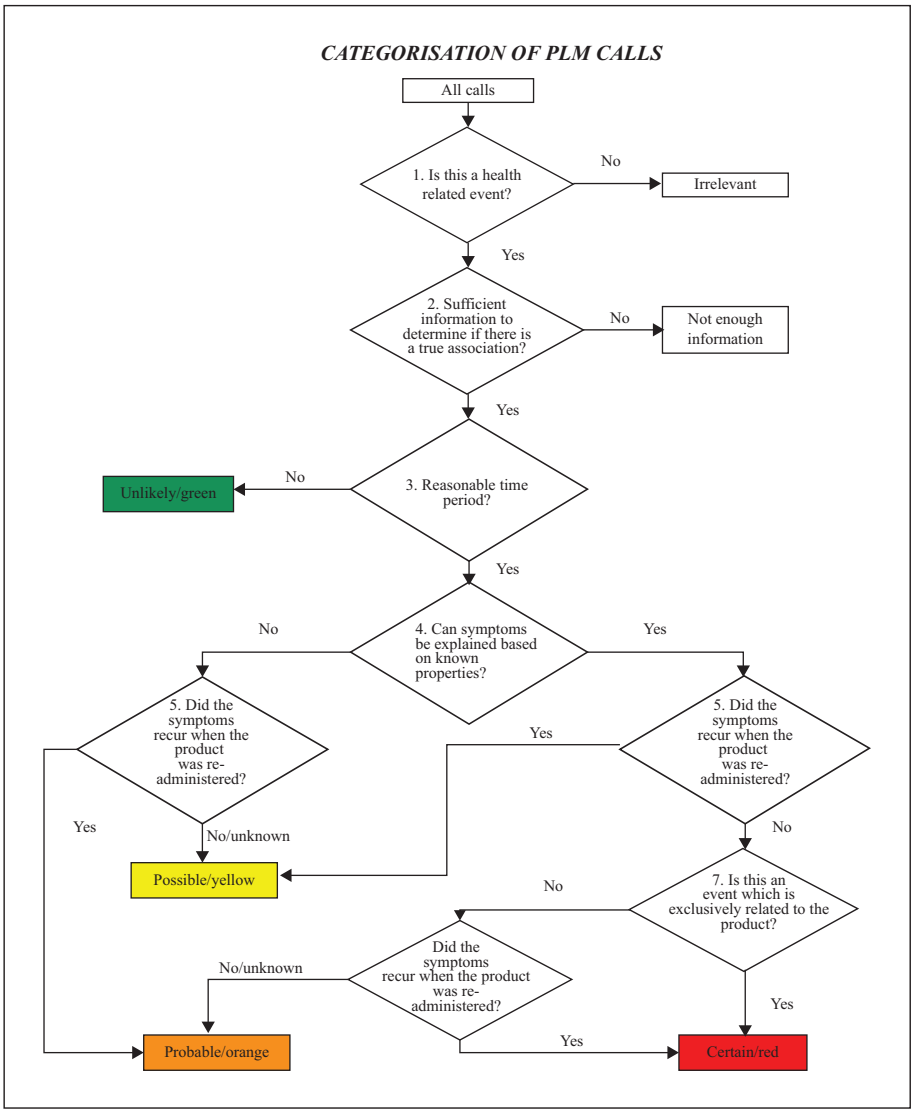


Figure 2. Causality assessment using categorisation.

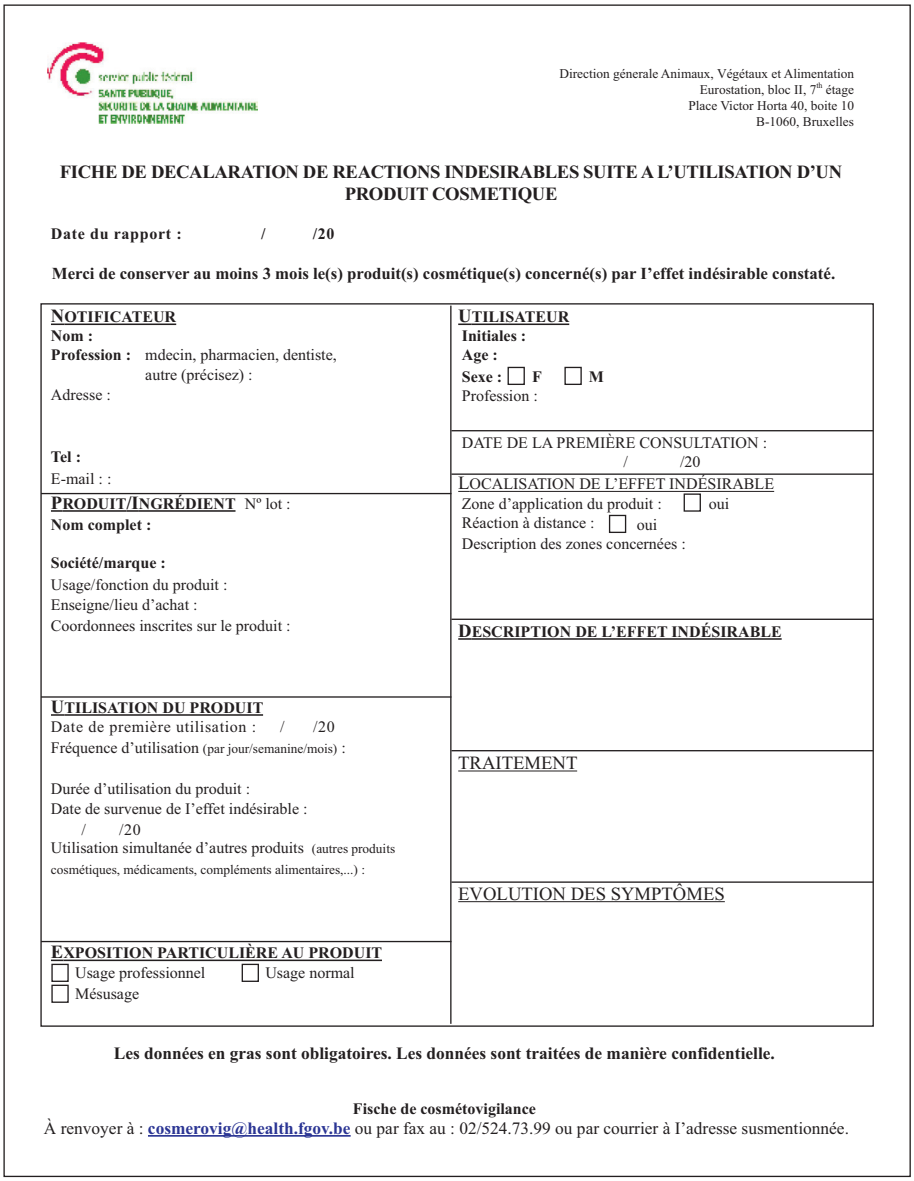
ical elements as well as detailed evolution over time. The notification must be carried out when the undesirable effect occurs and will then possibly be complemented later by the results of useful additional tests or by data on evolution. The same notification can be sent to the person responsible for marketing the product. Notification to Revidal-Gerda only occurs when the undesirable effect is an allergic undesirable effect; this notification can be carried out by any European dermatologist/allergist. Although the 2004 Public Health Law does not mention consumers, professional users and industrialists, it seems that they can also make reports on the ANSM website or on the websites of the competent authorities of Member States, as these websites provide specific tabs for them.

The use of alerts

All health care professionals can consult the latest ongoing warnings on the ANSM website and use this data to improve the management of their patients. Taking part in the Revidal-Gerda network enables health care professionals to remain updated on current allergen ingredients and also to use this data for better patient management. Regular reports transmitted to the cosmetic industry allow for product improvement.

Conclusion

Cosmetovigilance is a recent concept. The term itself has just been indexed. Revidal-Gerda and then AFSSAPS were at the forefront in this area. Authorities competent to receive notifications are currently being implemented. Europe is now convinced that cosmetovigilance systems are a genuine means of obtaining information on the safety of cosmetic products and their ingredients. They can be used by Europe to check that new directives ensure a high level of safety. Cosmetovigilance makes it possible to rule out or to control potentially hazardous ingredients and can thus set our minds at ease on the products placed on the market. ■



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Place Victor Horta 40, boite 10
B-1060, Bruxelles

FICHE DE DECALARATION DE REACTIONS INDESIRABLES SUITE A L'UTILISATION D'UN PRODUIT COSMETIQUE

Date du rapport : / /20

Merci de conserver au moins 3 mois le(s) produit(s) cosmétique(s) concerné(s) par l'effet indésirable constaté.

NOTIFICATEUR
Nom :
Profession : mdecin, pharmacien, dentiste, autre (précisez) :
Adresse :

Tel :
E-mail : :

PRODUIT/INGRÉDIENT N° lot :
Nom complet :

Société/marque :
Usage/fonction du produit :
Enseigne/lieu d'achat :
Coordonnees inscrites sur le produit :

UTILISATION DU PRODUIT
Date de première utilisation : / /20
Fréquence d'utilisation (par jour/semaine/mois) :

Durée d'utilisation du produit :
Date de survenue de l'effet indésirable :
/ /20
Utilisation simultanée d'autres produits (autres produits cosmétiques, médicaments, compléments alimentaires,...) :

EXPOSITION PARTICULIÈRE AU PRODUIT
☐ Usage professionnel ☐ Usage normal
☐ Mésusage

UTILISATEUR
Initiales :
Age :
Sexe : ☐ **F** ☐ **M**
Profession :

DATE DE LA PREMIÈRE CONSULTATION :
/ /20

LOCALISATION DE L'EFFET INDÉSIRABLE
Zone d'application du produit : ☐ oui
Réaction à distance : ☐ oui
Description des zones concernées :

DESCRIPTION DE L'EFFET INDÉSIRABLE

TRAITEMENT

EVOLUTION DES SYMPTÔMES

Les données en gras sont obligatoires. Les données sont traitées de manière confidentielle.

Fische de cosmétovigilance
À renvoyer à : cosmerovig@health.fgov.be ou par fax au : 02/524.73.99 ou par courrier à l'adresse susmentionnée.

Figure 3. Belgian cosmetovigilance notification form to report undesirable effects (similar to the one found on ANSM website).

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