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The use of non-animal alternatives in the safety evaluations of cosmetics ingredients by the Scientific Committee on Consumer Safety (SCCS)

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ABSTRACT

In Europe, the safety evaluation of cosmetics is based on the safety evaluation of each individual ingredient. Article 3 of the Cosmetics Regulation specifies that a cosmetic product made available on the market is to be safe for human health when used normally or under reasonably foreseeable conditions. For substances that cause some concern with respect to human health (e.g., colourants, preservatives, UV-filters), safety is evaluated at the Commission level by a scientific committee, presently called the Scientific Committee on Consumer Safety (SCCS).

According to the Cosmetics Regulations, in the EU, the marketing of cosmetics products and their ingredients that have been tested on animals for most of their human health effects, including acute toxicity, is prohibited. Nevertheless, any study dating from before this prohibition took effect is accepted for the safety assessment of cosmetics ingredients. The in vitro methods reported in the dossiers submitted to the SCCS are here evaluated from the published reports issued by the scientific committee of the Directorate General of Health and Consumers (DG SANCO); responsible for the safety of cosmetics ingredients. The number of studies submitted to the SCCS that do not involve animals is still low and in general the safety of cosmetics ingredients is based on in vivo studies performed before the prohibition.

1. Introduction

The safety evaluation of cosmetics in Europe is based on the evaluation of each individual ingredient. Article 3 of the European Cosmetics Regulations specifies that a cosmetic product made available on the market is to be safe for human health when used normally or under reasonably foreseeable conditions. Cosmetics products have rarely been associated with serious health hazards; however, this does not mean that the use of cosmetics per se is safe. Particular attention needs to be paid to long-term safety aspects, since cosmetics products may be used extensively over a large part of the human lifespan and sensitive groups of the population such as children, old people, pregnant women, etc., may be affected. Therefore, safety-in-use for cosmetics products has been established in Europe by controlling the ingredients via their chemical structures, toxicity profiles, and patterns of exposure.

The safety of those substances that cause some concern with respect to human health (e.g., colourants, preservatives, UV-filters, etc.) is evaluated at the Commission level by a scientific committee, presently called the Scientific Committee on Consumer Safety (SCCS). The substances are detailed in the Annexes of Regulation (EC) No. 1223/2009, which replaced the previous Directive from 11 July 2013 onwards (European Commission, 2009).

The SCCS was established in 2008 to substitute the former Scientific Committee of Consumer Products (SCCP). Before 1997, the recommendations proposed by the Scientific Committee on Cosmetology at the Commission's request were included in EC Reports. Between 1997 and 2004, all Scientific Committee opinions were published on the internet and can be accessed through the Committee's website. All SCCS opinions can easily be located through the substance category of the ingredient involved and the adoption date.

One of the responsibilities of the SCCS is to recommend guidelines for the cosmetics and raw materials industries to develop adequate studies for the safety evaluation of cosmetics. The SCCS evaluates the dossiers submitted by industry through the Directorate General of Health and Consumers (DG SANCO). The cosmetics ingredients evaluated by the SCCS correspond to those in the Annexes of the Regulations and to substances forbidden in Annex II, restricted substances in Annex II, and colourants, preservatives and UV-filters in Annexes IV, V and VI respectively.

Determination of the toxic potential of a cosmetics product is based on a series of toxicity studies and forms part of the hazard identification. Alternative methods, replacing animal testing, have

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been mandatory in Europe to evaluate cosmetics ingredients since March 2013, according to a Commission Decision. However, at present, the majority of toxicological tests still involve the use of animals, as is also the case for other chemical substances. Traditionally, toxicological data that are relevant to human health have been obtained by studying the toxicological profiles on animals of the substances under consideration, using the same exposure route as that in humans (topical, oral or inhalation).

When a dossier containing information on a cosmetics product is submitted to the SCCS for evaluation, the manufacturer should provide the Commission with information on: acute toxicity (if available); irritation and corrosivity to skin and eye; skin sensitisation; dermal/percutaneous absorption; repeat dose toxicity; mutagenicity/genotoxicity; carcinogenicity; reproductive toxicity; toxicokinetics; photo-induced toxicity; and human data (SCCS/1501/12).

One consideration before toxicological studies are accepted for evaluation is whether the studies have been carried out according to guidelines and following Good Laboratory Practice (GLP). In some cases, this information is not present and the SCCS asks for further information before making an opinion.

According to the Cosmetics Regulation (European Commission, 2009), it is prohibited in the EU to market cosmetics products and their ingredients if they have been tested on animals for most human health effects, including acute toxicity. This imposes on the cosmetics industry the need for alternative approaches to the safety testing of the ingredients of consumer products. After a meeting of experts organised by the European Centre for the Validation of Alternative Methods (ECVAM), the alternative methods that existed at the time and had been applied to cosmetics were reviewed (Adler et al., 2011; Hartung et al., 2011).

The 7th amendment to the EU Cosmetics Directive prohibits the launching of animal-tested cosmetics on the European market after 2013. The European Commission invited stakeholders (industry, non-governmental organisations, EU member states and the Commission's SCCS) to identify scientific experts in five areas of toxicological: toxicokinetics, repeat dose toxicity, carcinogenicity, skin sensitisation, and reproductive toxicity. The experts selected were asked to analyse the status of and prospects for alternative methods, and to provide a scientific estimate of the time necessary to achieve full replacement of animal testing. In short, the experts confirmed that it would take at least another 7–9 years for the complete replacement of the current in vivo animal tests used for the skin sensitisation safety assessment of cosmetics ingredients for skin sensitisation. However, the experts were also of the opinion that alternative methods may provide hazard information, i.e., to differentiate between sensitisers and non-sensitisers, before 2017. This would, however, not provide complete information on what safe exposure is, because the relative potency of a sensitiser would still not be known. For toxicokinetics, the timeframe was 5–7 years to develop the models still lacking to predict lung absorption and renal/biliary excretion; and even longer to integrate the methods to fully replace animal toxicokinetic models. For the systemic toxicological endpoints of repeat dose toxicity, carcinogenicity and reproductive toxicity, the time necessary for full replacement could not even be estimated (Adler et al., 2011).

CAAT-Europe assembled experts from Europe, America and Asia to design a scientific roadmap for future risk assessment approaches, considering that the animal use for cosmetics testing for the European market has been banned. The key recommendations proposed focused on improving existing methods, the combination of hazard testing and toxicokinetics predictions and the developing of integrated test strategies among others. Important points are the data quality, and the scientific background of a test method. Information from each test system should be mapped along adverse outcome pathways (Leist et al., 2014).

2. Methodology

The study material consisted of SCCS opinions issued between April 2008 and March 2013 concerning cosmetics ingredients. No confidential data were used, as all the information came from opinions downloaded from the Committee's website. There are different types of opinions and in some cases there are addenda to previous opinions. In this study, only full opinions were considered: addenda or specific opinions for a particular item, such as microbial resistance, were not taken into account.

Each opinion was analysed with respect to each of the different sections, taking note of whether the procedure used was based on the use of animals or non-animal models. The percentage of non-animal models was compared to that of animal models and the use of human data was also noted.

A total of 103 dossiers were analysed: 75 corresponded to hair dyes and 28 to other ingredients in cosmetics including UV filters, fragrances and preservatives, among others.

3. Results and discussion

SCCS opinions are currently organised into hair dyes, cosmetics ingredients and nanomaterials; but over the period evaluated in the present study, the opinions were organised into fragrances, hair dyes, preservatives, UV-filters and other substances. In this paper, for comparative purposes, we distinguish between hair dyes and other ingredients, but we have also grouped the two categories together. The number of SCCS opinions depends on the type of cosmetics; hair dyes were the most numerous with 75 substances evaluated.

Studies performed on animals could be included only if they were performed before the ban on animal use in March 2009, except for repeat dose studies which were permitted until March 2013. After that date, new studies were required not to use animals.

3.1. Acute toxicity

Studies of acute toxicity are not always necessary for the dossiers submitted to the SCCS, but they are usually included in those supplied by industrial sources and in all cases the studies were performed on laboratory animals. The oral route was the most common, but the dermal route was also used occasionally and in a few cases information about the inhalation route was also supplied. All the accepted methods for determining acute oral toxicity are based on in vivo experiments that estimate the LD50 value (i.e., the single dose of a substance that can be expected to cause death in 50% of the animals in an experimental group). Considering the prohibition on the use of animals for cosmetics ingredients and building on the results of a previous international validation study, a follow-up study was organised by the ECVAM to assess whether the 3T3 Neutral Red Uptake cytotoxicity assay could identify substances not requiring classification as acute oral toxicants under the EU regulations. The assay exhibited high sensitivity (92–96%) but relatively low specificity (40–44%). It could thus prove to be a valuable part of an integrated testing strategy: a read-across argument or weight-of-evidence (WoE) approach to identifying non-toxic chemicals (LD50 > 2000 mg/kg) (Prieto et al., 2013). In the dossiers supplied by industry sources for SCCS evaluation over the period 2009–2013, no assays to predict acute toxicity were performed in vitro.

3.2. Eye irritation

Eye irritation is one of the classic studies performed on animals, usually rabbits, as reported many years ago (Draize et al., 1944).