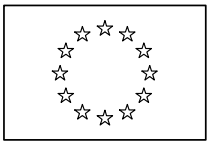

COMMISSION OF THE EUROPEAN COMMUNITIES

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REPORT FROM THE COMMISSION TO THE COUNCIL AND THE EUROPEAN PARLIAMENT

Report on the Development, Validation and Legal Acceptance of Alternative Methods to Animal Tests in the Field of Cosmetics (2007)

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1. INTRODUCTION

The present "Report on the Development, Validation and Legal Acceptance of Alternative Methods to Animal Experiments in the Field of Cosmetics" is the seventh report presented by the Commission. It reflects the state of play in terms of the number and type of experiments on animals relating to cosmetic products in 2005 and 2006, the current status of alternative replacement methods, and the acceptance and recognition of alternative methods at international level. The report is produced in order to comply with Article 9 of Council Directive 76/768/EEC of 27 July 1976 on the approximation of the laws of the Member States relating to cosmetic products (hereinafter "Cosmetics Directive"), as amended by the European Parliament and Council Directive 2003/15/EC of 27 February 2003. It is the third report on the basis of the 7th Amendment to the Cosmetics Directive and following the inclusion of the Protocol on the Welfare of Animals in the Treaty of Amsterdam in 1999.

2. NUMBER AND TYPE OF EXPERIMENTS RELATING TO COSMETIC PRODUCTS CARRIED OUT ON ANIMALS

2.1. Legal Background

According to Article 9 (a) of the Cosmetics Directive, every year the Commission shall present a report to the European Parliament and the Council on progress made in the development, validation and legal acceptance of alternative methods. The report shall contain precise data on the **number and type of experiments** relating to cosmetic products carried out on animals. The Member States shall be obliged to collect that information in addition to collecting statistics as laid down by Council Directive 86/609/EEC of 24 November 1986 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes (Experimental Animals Directive). The Experimental Animals Directive includes requirements to report at regular intervals not exceeding three years on the **number and kinds of animals** used in experiments.

The information to be provided under the Cosmetics Directive should enable the European Commission and the Member States to gain a complete picture of the situation in the field of animal testing in relation to cosmetic products. This information will be useful in order to apply the relevant provisions of the Cosmetics Directive.

The ban on the testing of finished cosmetic products has been in force since 11 September 2004, whereas the ban on testing ingredients or combination of ingredients will be implemented gradually as alternative methods are validated and adopted; however there will be a maximum cut-off date of six years after the entry into force of the Directive, i.e. 11 March 2009, irrespective of the availability of alternative non-animal tests. The marketing ban

will apply step by step as soon as alternative methods are validated and adopted in EU legislation, with due regard to the OECD validation process. This marketing ban will be introduced at the latest six years after entry into force of the Directive, i.e. by 11 March 2009, for all human health effects with the exception of repeated-dose toxicity, reproductive toxicity and toxicokinetics. For these specific health effects, a deadline of 10 years after entry into force of the Directive is laid down, i.e. 11 March 2013, regardless of the availability of alternative non-animal tests.

2.2. Animal Testing Data[1]

For the present report, 26 Member States supplied information on animal tests carried out for the safety of cosmetic products in 2005 and 2006. Despite several requests, Portugal did not transmit any information for this report under Article 9 (a) of the Cosmetics Directive. As mentioned in a reminder letter addressed to Member States, the Commission will consider opening infringement procedure.

According to the information submitted, cosmetic ingredients have only been tested on animals in the territories of France[2] and Romania. These Member States provided detailed information, including the testing period, the toxicological test endpoint, species of animals used for experiments and number of animals used for testing (Table 2).

In total, about 2 276 animals in 2005 and about 1329 animals in 2006 were used in tests carried out in relation to the safety of cosmetic ingredients (Table 1). The other 24 Member States reported that they did not perform such animal tests in their territory in 2005/2006 or that they cannot provide the information for the reasons explained below (see 3.b).

Number of animals used in Member States (2005/2006) – Table 1

	NUMBER OF ANIMALS USED		ANIMALS USED
	2005	2006	
ROMANIA	40	40	Rats
FRANCE	2236	1289	Mice, rats, guinea pigs, rabbits
Total	2276	1329	

[1] See reservations on the accuracy of data in paragraph 3 "Evaluation of submitted data"

[2] There are four laboratories which perform animal testing in France for cosmetic ingredients or combination of ingredients. Research protocols are done for French clients and client from one another Member State.

Number of Animals Used in Relation to Toxicological Endpoints (2005/2006) – Table 2

TYPES OF TESTS / COUNTRIES	ROMANIA		FRANCE	
	2005	2006	2005	2006
Skin irritation			165	248
Eye irritation			205	250
Skin sensitivity	40	40	1473	455
Photosensitivity			132	113
Oral toxicity			261	223

The total number of animals used for testing the safety of cosmetics showed a significant fall compared to the last report (2003: 1618, 2004: 8998). Indeed, the figures for 2006 are below those of 2003, even though twelve[3] new Member States joined the EU in that period.

As mentioned in the last report, the reported number of animals used for the testing of cosmetics or toiletries is still relatively small compared to the total number of animals used for experimental and other scientific purposes. The Fifth Report on the Statistics on the Number of Animals used for Experimental and other Scientific Purposes in the Member States of the European Union[4] mentioned that 8% of the total number of animals used for experimental purposes are used for toxicological and other safety evaluations, of which cosmetics represent 0.5%.

2.3. Evaluation of submitted data

In August 2007, the Commission asked Member States to send accurate data on the number and type of experiments relating to cosmetic products carried out on animals in 2005 and 2006 in accordance with Article 9 (a) of the Cosmetics Directive. The Commission specified that this information should also explain precisely what the figures represent and the way in which they were collated.

Furthermore, the Commission annexed to this request the guidelines announced in the 2005 Report in order to facilitate accurate generation and collation of animal testing data relating to cosmetic products.

2.3.1. Main explanations given by Member States:

The majority of Member States replied that no animal testing in relation to cosmetic products was performed in 2005 and 2006 in their territory. The main explanations they gave to substantiate their replies were the following:

– National legislation prohibits the carrying out of animal experiments in order to test and develop cosmetic products and their ingredients. Interestingly, sometimes some

[3] Bulgaria and Romania provided data, even if they joined afterwards.

[4] 5.11.2007, COM(2007) 675 final

Member States specify that testing for cosmetic purposes is prohibited within multiple use tests.

– National legislation stipulates that animal testing must be authorised in order to be lawfully performed, and therefore:

  – No authorisation was given to laboratories to test and develop cosmetic products and their ingredients;

  – There are no approved establishments for animal experiments relating to cosmetic products.

– The following do not exist on national territory

  – testing facilities for animal testing related to human health; or

  – laboratories complying with the requirements of good laboratory practice where non-clinical studies of the health and environmental safety of substances could be carried out.

– The authorities responsible for checking cosmetic products and carrying out market surveillance do not conduct or commission animal experiments for the purposes of such checks.

– A letter and a questionnaire were sent to representatives of cosmetic product manufacturers.

– Competent authorities checked the product information file which, according to Article 7a, paragraph 1(h) of the Cosmetics Directive, must contain "*data on any animal testing performed by the manufacturer, his agents or suppliers, relating to the development or safety evaluation of the product or its ingredients, including any animal testing performed to meet the legislative or regulatory requirements of non-member countries*". They found nothing to suggest that chemical substances used as ingredients in cosmetics had been tested on animals.

2.3.2. Details of difficulties encountered by Member States

Some Member States elaborate on their replies by mentioning the difficulties they had in collecting the information.

As mentioned in the previous report, chemicals are rarely tested on animals solely for their use as ingredients in cosmetics, and the majority of animal tests are conducted for multiple uses by manufacturers of chemical substances (industry assumes that approximately 80-90% of cosmetic ingredients are tested for multiple uses). Therefore, some Member States acknowledged that it is difficult to determine which results of which research may subsequently be referred to by the cosmetic industry.

Sweden explained that it considers itself unable to provide the requested information, as in its view it does not have the legal basis to make such a request to companies. Indeed, the information provided according to Article 7a, paragraph 1(h) is only required to be readily accessible to the competent authorities of the Member State.

2.3.3. Initiatives taken by Member States for the collection of data

In view of the situation and the efforts requested of the Member States by the Commission to deliver the appropriate information, some Member States did provide information about the initiatives considered:

– In order to ensure greater transparency in the data received, the toxicology laboratory that normally carries out the most tests for third parties has initiated an internal procedure under which clients are required to declare that the substances sent for testing will not be used as ingredients in cosmetic products.

– The supplier or manufacturer or the person responsible for placing the cosmetic product on the market shall inform the National Chemicals Bureau about the types and number of tests they have conducted on animals in connection with the purpose of ensuring their suitability and compliance with the cosmetic legislation.

– In order to simplify data collection, the possibility of making it obligatory for manufacturers to submit information on tests carried out on animals once a year is being examined.

2.3.4. Conclusion

The Commission continues to be concerned about the accuracy of the figures being reported, and this concern is shared by Member States.

The main issue relates to multi-use substances. Interestingly, some Member States, when mentioning that no animal testing has been performed for cosmetic products, reported that no toxicological tests were carried out for multiple or uncertain purposes where it could be considered that the substance might be used as an ingredient in cosmetic products.

The Commission considers that the best available source for information at national level is the information held according to Article 7a (1) (h). It is also the most suitable way to enforce the marketing ban laid down in Article 4a of the Cosmetics Directive. The implementation of REACH[5] would allow passing this information to the downstream user of the ingredient. Within this context, the Commission will consider how further improve the availability of relevant information.

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[5] Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC, OJ L 396 of 30.06.2006 p. 1.

3. PROGRESS IN THE DEVELOPMENT, VALIDATION AND LEGAL ACCEPTANCE OF ALTERNATIVE METHODS

3.1. Legally Accepted Replacement Methods

3.1.1. Under Annex IX of the Cosmetics Directive

Annex IX of the Cosmetics Directive "lists the alternative methods validated by the European Centre on Validation of Alternative Methods (ECVAM) of the Joint Research Centre available to meet the requirements of this Directive and which are not listed in Annex V to Council Directive 67/548/EEC on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances".

The purpose of Annex IX of the Cosmetics Directive is to supplement Annex V of Council Directive 67/548/EEC. Annex IX was created in order to ensure, without delay, the regulatory acceptance of alternative methods that would not be applicable to the whole chemical sector, but only to the cosmetic sector. Indeed, recital 5 of Directive 2003/15/EC of the European Parliament and of the Council provides the following background: "Currently [in 2003], only alternative methods which are scientifically validated by the European Centre for the Validation of Alternative Methods (ECVAM) or the Organisation for Economic Cooperation and Development (OECD) and applicable to the whole chemical sector are systematically adopted at Community level. However, the safety of cosmetic products and their ingredients may be ensured through the use of alternative methods which are not necessarily applicable to all uses of chemical ingredients. Therefore, the use of such methods by the whole cosmetic industry should be promoted and their adoption at Community level ensured, when such methods offer an equivalent level of protection to consumers".

Considering that ECVAM did not validate alternative methods to animal testing that would not be applicable to the whole chemical sector, Annex IX was not amended in 2007 and is still empty.

3.1.2. Under Annex V of Council Directive 67/548/EEC

The adoption of the 30th adaptation to technical progress of Council Directive 67/548/EEC, amending in particular Annex V, has been delayed due to the procedure under the Technical Barriers to Trade agreement.

This draft Directive provides for an update of the following methods which were already listed:

– B. 40. *In vitro* skin corrosion: transcutaneous electrical resistance test (TER), equivalent to the OECD TG 430 (2004);

– B. 40 Bis. *In vitro* skin corrosion: human skin model test, equivalent to the OECD TG 431 (2004);

– B. 41. *In Vitro* 3T3 NRU phototoxicity test, equivalent to OECD TG 432 (2004);

And for the introduction of the following method concerning skin absorption:

– B. 45. skin absorption (skin penetration): *in vitro* Method, equivalent to the OECD TG 428 (2004).

3.1.3. Under the Commission Regulation on the adoption of testing methods under Regulation 1907/2006 (the "REACH" Regulation)

Directive 2006/121/EC[6] of the European Parliament and of the Council provides for the deletion of Annex V of Council Directive 67/548/EEC as from 1 June 2008. The Commission has therefore adopted an implementation Regulation under REACH, which brings together, in one Regulation, all the test methods contained in Annex V to Directive 67/548/EEC[7].

3.2. Progress in Development and Validation of Alternative Approaches

3.2.1. ECVAM Technical Report

The European Centre for the Validation of Alternative Methods (ECVAM) of the EC's Joint Research Centre (JRC) prepared a "Cosmetics Technical Report" which is published in annex to this report. Although the figures in this report cover the period 2005-2006, the technical report also covers the year 2007. It assesses the possibility of fully replacing animal tests before the cut-off dates set out in Article 4a of the Cosmetics Directive.

3.2.1.1. For the end points falling under the 2009 deadline

For skin corrosion, acute phototoxicity and skin penetration, as mentioned in the 2005 report, accepted replacement assays already exist.

For in vitro skin irritation testing, ECVAM declared as scientifically validated an assay based on reonstituted human epidermis (EPISKIN ™) in April 2007. This method is currently undergoing regulatory acceptance in the EU.

For mutagenicity, in vitro methods have already been incorporated in legislation[8]. However, under the current test strategy for genotoxicity, positive results obtained from these methods require confirmation by animal testing due to the fact that they produce a high number of false positives. Although the primary screening of substances is based on in vitro methods, the deadline of 2009 might still pose a problem. Indeed, owing to the existence of false positives, which cannot be reduced in the absence of alternative methods to animal testing for the confirmation of results, the number of active cosmetic ingredients would be reduced, for reasons not linked to their safety.

For eye irritation, the 2009 deadlines for full replacement are unlikely to be met. The validated tests and tests strategies available would allow only for the partial replacement of the animal test. Therefore, research is ongoing in order to allow such a replacement in future.

For acute toxicity, because the results of the DG RTD funded A-cute-Tox EU project will not be available until 2009 results will not become available until 2010 onwards.

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6 Directive 2006/121/EC of the European Parliament and of the Council of 18 December 2006 amending Council Directive 67/548/EEC on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances in order to adapt it to Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) and establishing a European Chemicals Agency, OJ L 396 of 30.12.2006.

7 OJ L 142 of 31.05.2008

8 In Annex VIII of Regulation 1907/2006 REACH

3.2.1.2. For the endpoints falling under the 2013 deadline

As already mentioned in the 2005 report, there is unfortunately no indication that the deadline can be met for the complex endpoints, such as chronic toxicity, reproductive toxicity and toxicokinetics, although several activities are ongoing. The only area for optimism would appear to be skin sensitisation, depending on the results of the integrated project Sens-it-iv.

3.2.2. SCCP statements

In 2007, the Scientific Committee on Consumer Products (SCCP), who is responsible for the evaluation of the substance used in cosmetic products, delivered, on its own initiative, two statements regarding the availability of alternative methods.

In its memorandum of June 2007 on the Actual Status of Alternative Methods on the Use of Experimental Animals in the Safety Assessment of Cosmetic Ingredients in the European Union[9], the SCCP expressed its concerns regarding the availability of alternative methods to animal testing to conduct safety assessment, opposed to hazard identification.

In its memorandum of December 2007[10]on the *in vitro* test EPISKIN™ for skin irritation testing, the SCCP underlined the possible limited applicability of this method regarding colouring agents and hair dyes. This aspect was mentioned by ECVAM when transmitting this method for regulatory acceptance under Annex V of Council Directive 67/548/EEC.

3.2.3. RTD activities

Developing robust and effective, novel, alternative methods has been a priority under the Framework Research Programmes of the European Union for more than 20 years. The first calls for proposals under the 7th RTD Framework Programme resulted in the selection of five proposals on the Theme "Health" (two large–scale integrating projects, two focused research projects, and one specific support action, expected EU contribution: €30 million). The areas addressed by the Theme "Health" include: profiling the toxicity of new drugs and of nanoparticles in medical diagnostics without animal tests, QSAR models in the field of predictive toxicology and bottlenecks in the 3R approach in pharmaceutical development.

Two proposals have been selected for funding in the Theme "Environment" (2 focused research projects in the field of in-silico methods; expected EU contributions: €5 million). Even though the projects are tailor-made for specific areas, it is expected that their results will be widely transferable to other areas relevant for the implementation of the 3R concept.

3.2.4. COLIPA (The European Cosmetic Toiletry and Perfumery Association)

It has a research programme on Alternative Approaches to Animal Testing (AAT) to support the development, validation and acceptance of alternative approaches in order to replace animal use.

For eye irritation, COLIPA submitted to ECVAM in beginning of 2008 results from the optimization of the two most advanced Human Reconstructucted Tissue models[11].

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9 SCCP/1111/07; http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_s_06.pdf

10 SCCP/1145/07; http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_s_07.pdf

11 SkinEthic Human Corneal Epithelium (HCE) model and the MatTek Epiocular model

For genotoxicity and mutagenicity, COLIPA is working to develop approached to reduce the "false positive" rate of in vitro mammalian cell genotoxicity assays and to develop genotoxic assays in 3D human skin models.

For skin allergy, COLIPA is aiming to propose three methods for validation to ECVAM in 2008[12].

3.2.5. Others

The ongoing activities mentioned in the 2005 report, such as the European Partnership for Alternative Approaches to Animal Testing (EPAA)[13] the Community Action Plan on the Protection and Welfare of Animals[14] and the revision of Directive 86/609/EEC on the protection of animals used in experiments[15], were continued.

4. ACCEPTANCE AND RECOGNITION OF ALTERNATIVE METHODS AT INTERNATIONAL LEVEL

The Commission has put the issues of validation and regulatory acceptance of alternative methods at the top of its agenda of sectoral regulatory dialogues at both multilateral and bilateral level.

4.1. Multilateral level

The Commission met with its counterparts from the United States, Japan and Canada at the "International Cooperation on Cosmetic Regulation" ("ICCR") meeting from 26 to 28 September 2007. One focal point of this meeting was exploring hurdles in the international regulatory acceptance of alternative testing methods. It was concluded that it is therefore crucial to ensure that, at the validation stage, the assessments within different jurisdictions do not differ.

An agreement at the "validation stage" would be a great help in ensuring harmonised regulatory acceptance, thus facilitating trade and enhancing animal welfare.

In order to avoid different recommendations after validation and peer review of alternative methods/approaches, the Commission is working towards establishing an international collaboration on validation/peer review processes in various regions. Discussions have started between the EU and US in the framework of the Transatlantic Economic Council (see below).

In addition to these efforts, the Commission is cooperating with the OECD by, regularly taking part in meetings and working groups, such as the OECD Working Group of the National Coordinators of the Test Guidelines Programme, the Endocrine Disrupters Testing and Assessment Task force and its subgroups, that deal with non-animal tests (e.g. Validation Management Group - Non-Animal), and other ad-hoc expert groups dealing with various alternative methods.

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12 Human Cell Line Activation Test (h-CLAT), U937/CD86 and a pepttide-binding assay.

13 For further information see http://www.ec.europa.eu/enterprise/epaa/index_en.htm

14 COM (2006) 13 final, 23.1.2006

15 For further information see http://ec.europa.eu/environment/chemicals/lab_animals/revision_en.htm

4.2. Bilateral level

Questions of validation and regulatory acceptance of alternative methods are also at the core of the various bilateral regulatory dialogues with the main trading partners. In particular:

4.2.1. U.S.

Making progress on issues of validation and regulatory acceptance of alternative methods is one of the key deliverables agreed under the Transatlantic Economic Framework, and this work is closely monitored by the Transatlantic Economic Council (TEC).

The issue was discussed at the meeting with the TEC on 9 November 2007 in Washington between Vice-President Günter Verheugen and the then Director of National Economic Advisors/Special Assistant to the US President, Al Hubbard.

The EU and the United States agreed that the approach chosen at the multilateral level (see above) is crucial and are working towards the swift establishment of a joint validation/peer review process taking into account the specific demands of different jurisdictions as far as possible.

ECVAM and IICVAM are collaborating on several validation studies and ICCVAM has an observer status on the EVCAM Scientific Advisory Committee (ESAC).

ICCVAM also participated in the annual conferences of EPAA in 2006 and 2007.

4.2.2. Japan

In Japan, animal testing of cosmetic products and their ingredients is not obligatory *per se*. However, animal tests are conducted in the framework of the regulation of cosmetics ingredients and "quasi-drugs", some of which are considered as cosmetic products in the EU.[16]

Issues of animal testing have been repeatedly raised, particularly in the framework of the regulatory reform dialogues in 2006 and 2007. In 2006, Japan stressed its commitment to implement OECD testing guidelines. In 2007, Japan indicated a clear interest in participating in the setting-up of an international validation process as discussed at the ICCR (see above).

Moreover, activities in the field of validation are also ongoing under the co-ordination of JaCVAM (Japanese Centre for the Validation of Alternative Methods). ECVAM is an official member in the validation management teams whereas observers from JaCVM are regulatory invited to meetings of the ECVAM Scientific Advisory Board (ESAC).

4.2.3. China

The regulatory system in China is particularly challenging, as animal testing on the finished cosmetic product is obligatory in order to have market access. These tests are often carried out by the competent authorities under a marketing authorisation.

The issue has been discussed in numerous fora, and in particular at

[16] For example, deodorants, hair dyes and certain oral care products.

– the EU-China (AQSIQ) working group on cosmetic products which met on 15 September 2006 in Brussels and on 24 October 2007 in Beijing. At the invitation of the Commission, AQSIQ also participated at the second annual conference of EPPA on 18 December 2006.

– the meeting of the Commission with the Chinese SFDA on 4 July 2007 in Brussels;

Moreover, questions about animal testing were raised in several comments by the EU on notifications under the TBT agreement.[17]

5. CONCLUSION

It can be noted that Member States have improved their internal structure in order to provide for accurate animal testing data and effective monitoring of the application of the testing and marketing bans, as it was encouraged in the guidelines annexed to the request to Member States for accurate data[18].

There are currently four alternative in vitro methods in relation to three toxicological endpoints (skin corrosion, acute phototoxicity and skin penetration) listed in Annex V of Directive 67/548/EEC and one method for the mutagenicity testing listed under REACH[19]. These alternative test methods are currently the only legally accepted tests at Community level aimed at fully replacing animal tests for toxicological endpoints in the area of chemicals and cosmetic products. A method concerning skin irritation is likely to be soon accepted for regulatory purposes. For eye irritation and acute toxicity, the situation is uncertain and the Commission will focus its efforts on these human health effects in view of the 2009 deadline.

For the 2013 deadline, the situation is much more critical. The replacement of animal test methods by alternative methods in relation to complex toxicological endpoints remains scientifically difficult, despite the additional efforts launched at various levels.

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17 Cf. in particular notification G/TBT/N/CHN/209 - Hygienic specifications for cosmetics.

18 See paragraph 2.3.

19 Listed under Annex VIII of Regulation 1907/2006.