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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 (2005)**

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I. INTRODUCTION

The present “Report on the Development, Validation and Legal Acceptance of Alternative Methods to Animal Experiments in the Field of Cosmetics” is the sixth report presented by the Commission. It reflects the state of play on the number and type of experiments on animals relating to cosmetic products in 2004, the current status of alternative replacement methods as well as the acceptance and recognition of alternative methods at the international level. The report is produced in order to comply with Art. 9 of the Council Directive 76/768/EEC of 27 July 1976 on the approximation of the laws of the Member States relating to cosmetic products (Cosmetics Directive), as amended by the European Parliament and Council Directive 2003/15/EC of 27 February 2003. It is the second report on the basis of the 7th Amendment to the Cosmetics Directive and after the inclusion of the Protocol on the Welfare of Animals in the Treaty of Amsterdam in 1999.

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

1. Legal Background

According to Art. 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 (Laboratory Animals Directive). The Laboratory Animals Directive includes reporting requirements at regular intervals not exceeding three years on the **number and kinds of animals** used in experiments.

The information to be provided in accordance with the Cosmetics Directive should enable the European Commission and the Member States to get a complete idea of the situation in the field of animal testing in relation to cosmetic products. This information will be useful to apply the provisions of the Cosmetics Directive on this matter.

The testing ban on finished cosmetic products applies since 11 September 2004, whereas the testing ban on ingredients or combination of ingredients will apply step by step as soon as alternative methods are validated and adopted, but with a maximum cut-off date of 6 years after 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 6 years after entry into force of the

Directive, i.e., 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 foreseen, i.e., 11 March 2013, irrespective of the availability of alternative non-animal tests.

2. Animal Testing Data

a) For the present report, 23 Member States² conveyed information on animal tests carried out for the safety of cosmetic products in 2004. EL and UK did not transmit any information for this report pursuant to Art. 9 (a) of the Cosmetics Directive. Both Member States have repeatedly informed the European Commission in the past that they are not carrying out animal tests for the development and safety assessment of cosmetic products.

According to the information submitted, cosmetic ingredients have been tested on animals in the territories of FR, DK and ES only. However, as in the last report, these Member States have not indicated the number of animal tests performed but instead the number of animals used. Also, these figures refer to “main uses” of substances in cosmetics or toiletry articles.

In total, about 9000 animals were used in tests carried out for the safety of cosmetic products (Table 1). The other 20 Member States reported that they did not perform such animal tests in their territory in 2004.

Number of animals used in Member States (2004) – Table 1

	NUMBER OF ANIMALS USED	ANIMALS USED
France	5496	Mice, rats, guinea pigs, rabbits
Denmark	12	Rats
Spain	3480	Mice, rats, guinea pigs, rabbits

Compared to the last report, the total number of animals used for testing the safety of cosmetics increased significantly (2003: 1618). At the same time, the market for cosmetics has continued to grow by 1 % compared to 2004. Sales for the 15 “old” Member States, Switzerland and Norway reached 60 billion Euro (retail sales prices) in 2005³.

There are several reasons for this increase in the number of animals used in the area of cosmetics. First, Spain did not transmit animal testing data in 2003, but did so for 2004. The increase of animals used in tests in France from about 1600 in 2003 to about 5500 in 2004 is caused, according to the French authorities, mainly by three additional test protocols carried out by two laboratories, two of which have been carried out for a French client and the other one for a client in another EU Member State.

¹ See reservations on the accuracy of data in paragraph 3 “evaluation of submitted data”

² Bulgaria and Romania were not involved in the reporting system

³ COLIPA, Annual Market 2005, June 2006, page 5

However, the reported number of animals mainly used for cosmetics or toiletries is still relatively small compared to the total number of animals used for experimental and other scientific purposes. The total number of animals used in the “old” fifteen EU Member States in 2002 was 10.7 Million according to the “Fourth Report on the Statistics on the Number of Animals used for Experimental and other Scientific Purposes in the Member States of the European Union (2002)⁴”.

b) For the first time, the Commission received information on the type of animal experiments performed in Member States. FR and ES submitted testing data in relation to the various toxicological endpoints (Table 2). For some types of animal tests, however, it remains unclear for what kind of human health effects they have been tested (“others”).

Number of Animals Used in Relation to Toxicological Endpoints (2004) – Table 2

TYPES OF TESTS / COUNTRIES	FRANCE	SPAIN	DENMARK
Tests of non lethal toxicity methods	629	No data	No information
Skin irritation	283	No data	No information
Skin sensitisation	875	1282	No information
Eye irritation	115	No data	No information
Subchronic and chronic toxicity	1279	1242	No information
Carcinogenicity	418	No data	No information
Development Toxicity	231	No data	No information
Mutagenicity	206	No data	No information
Reproductive Toxicity	310	No data	No information
Others	998	801	No information

3. Evaluation of submitted data

⁴ COM (2005) 7 of 20.01.2005

a) Reporting of animal testing data under the Cosmetics Directive has slightly been improved compared to the last report, although a number of questions and shortcomings remain. This again highlights the Commissions' continued concerns about the accuracy of the figures being reported.

After publication of the last annual report, the Commission has undertaken a number of efforts to clarify the situation and to assist Member States in collating accurate figures in relation to animal testing data. The Commission contacted Member States and other relevant stakeholders to clarify the collation of animal testing data, in particular with a view to animal tests carried out for multiple uses.

Several discussions with industry, animal welfare organisations and other stakeholders showed that:

- chemicals are rarely tested on animals solely for their use as ingredients in cosmetics,
- the majority of animal tests are carried out for multiple uses by manufacturers of chemical substances (industry assumes that approximately 80-90% of cosmetic ingredients are tested for multiple uses),

The Commission also provided Member States with guidance on the interpretation of the reporting requirements laid down in Art. 9 (a) of the Cosmetics Directive and discussed ways and means of gathering complete and accurate animal testing data in the field of cosmetics.

b) The information the Commission received from Member States for the present report demonstrates how difficult it is to generate accurate figures on animal testing in the field of cosmetics. Data on animal tests relating to cosmetic products are collated and generated differently throughout the European Union. There is no uniform practice to collate animal testing data in an accurate manner. In particular, the collation of relevant multiple use tests remains a significant problem.

Member States are confronted with two different reporting systems relating to the use of laboratory animals, namely the Laboratory Animals Directive 86/609/EEC and the Cosmetics Directive 76/768/EEC. The Cosmetics Directive has established much more ambitious reporting requirements than the Laboratory Animals Directive and Member States still have difficulties to adapt to this situation.

It can be assumed that the current situation does not fully provide for the collection of accurate data required under the Cosmetics Directive due to practices at national level. Some Member States

- collate data on the basis of an authorisation-/notification-procedure for animal tests, but these procedures do not ensure concrete information on the number and type of animal tests carried out in relation to cosmetic products;
- collate animal testing data according to "main uses" on the basis of Art. 13 of the Laboratory Animals Directive 86/609/EEC;

- request animal testing data from cosmetic companies although there is no downstream information on animal testing data from the chemicals manufacturer or other suppliers to the cosmetics manufacturer;
- claim that, according to their national legislation, animal tests are prohibited for the development of cosmetic products; this information, however, does not clarify how Member States break down figures for multiple use tests, which can include cosmetics use.

c) It is up to each Member State to establish an internal structure enabling it to collate and transmit to the European Commission precise data on the number and type of experiments relating to cosmetic products carried out on animals. Member States have the choice to establish their own mechanisms to collate animal testing data. However, these mechanisms shall ensure that all relevant test data are collated and transmitted to the European Commission for publication in the annual report. The European Commission is currently working on guidelines in order to facilitate accurate generation and collation of animal testing data relating to cosmetic products.

III. Progress in the Development, Validation and Legal Acceptance of Alternative Methods

1. Legally Accepted Replacement Methods

There are currently four alternative in vitro methods in relation to two toxicological endpoints (skin corrosion and acute phototoxicity) listed in Annex V of Directive 67/548/EEC. These alternative test methods are currently the only legally accepted tests at Community level aiming at fully replacing animal tests for toxicological endpoints in the area of chemicals and cosmetics.

The in vitro tests for skin corrosivity and the in vitro 3 T 3 NRU phototoxicity test were introduced into Part B (B. 40 and 41) of Annex V to Directive 67/548/EEC by Directive 2000/33/EC of 25 April 2000 and are to be applied in the framework of the testing and marketing bans under the Cosmetics Directive since 11 September 2004 (Art. 3 of Directive 2003/15/EC).

2. Progress in Development and Validation of Alternative Approaches

a) On 1 October 2004, the Commission established the timetables for the phasing-out of animal testing according to Art. 4 a §2 of the Cosmetics Directive. In order to estimate the time necessary to achieve full replacement of animal testing in the field of cosmetics, the Commission set up an Ad Hoc Group with representatives from industry, academia, animal welfare groups and governmental bodies that agreed on a “Report Prepared in the Context of the 7th Amendment of the Cosmetics Directive for Establishing the Timetable for Phasing Out Animal Testing”⁵. The Ad Hoc Working Group was re-launched in 2005 to monitor the progress on development, validation and legal acceptance of alternative methods to animal tests for cosmetic products. As a contribution to this process, the European Centre for Validation of Alternative Methods (ECVAM) of the EC’s Joint Research Centre (JRC)

⁵ ATLA, Vol.33, Supplement 1, July 2005

prepared a “Cosmetics Technical Report” which was submitted to Member States and all relevant stakeholders for consultation⁶.

The “Cosmetics Technical Report” assesses the possibility to fully replace animal tests before the cut-off dates provided by Art. 4 a of the Cosmetics Directive in a differentiated manner:

- The concerted activities seem promising for meeting the 2009 deadline. For skin corrosion, acute phototoxicity and skin penetration, accepted replacement assays already exist, whereas for mutagenicity accepted partial replacement assays exist. Results from a validation study on acute skin irritation look promising for meeting the deadline. Significant progress is also being made in the areas of eye irritation although additional work is still needed in order to fully replace the animal test. For acute toxicity, the results of a completed validation study indicate the possibility to identify non-toxic substances without the use of animals. Furthermore, as a result of the FP6 integrated project A-Cute-Tox (2005-2010) the proportion of substances, for which acute toxicity can be established, might be expanded in the near future.
- For the 2013 deadline, the situation is much more critical. It is highly unlikely that it will be possible to predict chronic toxicity with any test strategy or battery of non-animal tests. For reproductive toxicity some opportunities from the ReProTect project (2004-2009) might emerge. Cancer bioassays are very unlikely to be requested for cosmetic ingredients, since chemicals identified as positive in mutagenicity/genotoxicity assays are usually abandoned. However, in case the carcinogenic potential needs to be evaluated, cell transformation assays, which are currently under validation, might be used. Promising alternative methods exist for skin and respiratory sensitisation (currently tests under validation might allow the identification of large parts of non-sensitizers), and the integrated project Sens-it-iv seeks for new methods (2005-2010).

b) During the reporting period, increased efforts and numerous activities have been launched at EU-level to promote alternative approaches to animal testing. Most of them are of a more general nature but cover also the cosmetics sector.

- Developing robust and effective novel, alternative methods is a priority under the Framework Research Programmes of the European Union since more than twenty years. Between 1999 and 2002, the EU supported 43 research projects with 65 million Euro, several of which are still ongoing. In the current 6th Framework Programme on Research and Development, 20 projects were awarded with 80 million Euro by the Health Programme, and two projects on Intelligent Testing Strategies for chemicals and (Q)SARs, for about 12 Million Euro were awarded by the Global Change and Ecosystems Programme. Research activities will continue under 7th Framework Research Programme (2007-2013) through a coordinated activity on alternative methods and strategies for safety testing on pharmaceuticals and cosmetics (in the Health Programme) as well as industrial chemicals (in the Environment Programme).

⁶ The “Cosmetics Technical Report” as well as stakeholder- and additional ECVAM-comments are available on http://ec.europa.eu/enterprise/cosmetics/html/cosm_animal_test.htm.

- On 7 June 2006, the Commission adopted a Recommendation Establishing Guidelines on the Use of Claims referring to the Absence of Tests on Animals pursuant to Council Directive 76/768/EEC⁷. Further activities in relation to alternative approaches to animal testing have been launched at EU level, such as the European Partnership for Alternative Approaches to Animal Testing (EPAA)⁸, the Community Action Plan on the Protection and Welfare of Animals⁹, the revision of the Laboratory Animals Directive 86/609/EEC¹⁰ and the revision of SCCNFP's Notes of Guidance for the Testing of Cosmetic Ingredients and their Safety Evaluation.
- Private initiatives, such as those by the European Consensus-Platform for Alternatives (ECOPA)¹¹ and the Steering Committee on Alternatives to Animal Testing of the European Cosmetic Toiletry and Perfumery Association (SCAAT), also play a crucial role in promoting alternative test methods. Since 1992, SCAAT's main mission is the coordination of the Cosmetics Industry's efforts in the development and acceptance of alternatives to animals in cosmetic safety evaluation. It's work is based on collaboration – not only between member companies – but also with other groups who have a legitimate interest in the outcome of the research (academia, industrial trade associations, national research and regulatory bodies). Research comprises the understanding of biological mechanisms, method/strategies development, method optimisation, as well as prevalidation and validation in collaboration with ECVAM. The Colipa / SCAAT research programme focuses on the main areas of needs and expertise: skin and eye irritation, skin allergy, genotoxicity and risk assessment methodology¹².

⁷ OJ L 158 of 10.06.2006, page 18

⁸ For further information see http://www.ec.europa.eu/enterprise/epaa/index_en.htm

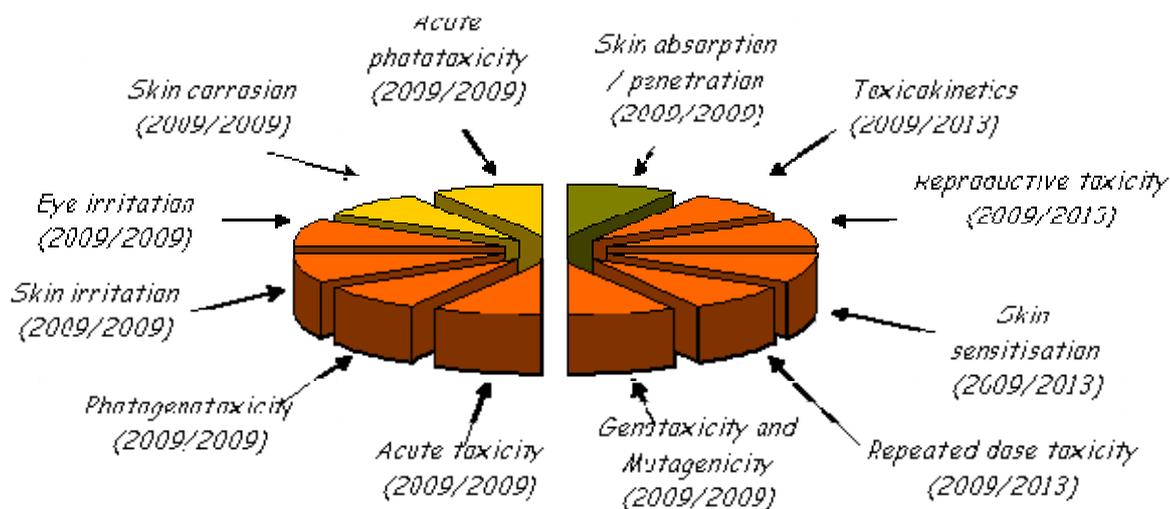
⁹ COM (2006) 13 final, 23.1.2006

¹⁰ For further information see http://ec.europa.eu/environment/chemicals/lab_animals/revision_en.htm

¹¹ For further information see <http://www.ecopa.eu/>

¹² For further information in this context see the “COLIPA Contribution” to the “Cosmetics Technical Report” of ECVAM http://ec.europa.eu/enterprise/cosmetics/html/cosm_animal_test.htm

Development, Validation and Acceptance of Alternative Methods in relation to Toxicological Endpoints applicable in the area of Cosmetics (State of Play) – Table 3¹³



Validated and legally accepted methods aiming at fully replacing animal tests for the relevant toxicological endpoints¹⁴



Validated methods aiming at fully replacing animal tests for the relevant toxicological endpoints



Alternative methods under development and/or under validation by ECVAM.

IV. ACCEPTANCE AND RECOGNITION OF ALTERNATIVE METHODS AT INTERNATIONAL LEVEL

1. Multilateral Level

OECD might play the most prominent role in promoting and accepting alternative methods at international level. OECD Test Guidelines (TG) are broadly accepted by the international scientific community and by appropriate regulatory authorities of OECD Member countries

¹³ 1st figure in brackets represents the cut-off date for the testing ban in relation to the respective toxicological end point (Art. 4 a para 1d of the Cosmetics Directive) ; 2nd figure represents the cut-off date for the marketing bans in relation to the respective toxicological end point (Art. 4 a para 1 a and b of the Cosmetics Directive)

¹⁴ Validated and legally accepted alternative methods are also available in relation to other toxicological endpoints, such as genotoxicity and mutagenicity, but these methods are not designed to fully replace animal testing for the relevant endpoints.

and a number of Non-Member countries. The EC-DG JRC's ECVAM is closely working with the OECD in the validation, acceptance and promotion of alternative methods.

In 2004, OECD adopted for the first time alternative methods aiming at replacing animal tests (skin absorption, TG 428; skin corrosion, TG 430 and 431; phototoxicity, TG 432).

2. Bilateral Level

The EU takes also a leading role in the international regulatory dialogues with authorities in USA and Japan in order to facilitate the compatibility of cosmetics regulations and to avoid trade conflicts. A key element of the EU-US cooperation is the implementation of the Guidelines for Regulatory Cooperation and Transparency agreed in June 2002 under the Transatlantic Economic Partnership (1998) in the framework of the New Transatlantic Agenda (1995).

In the 2005 roadmap for US-EU Regulatory Cooperation the EU and the US agreed that “the cooperation on the development of alternative methods needs further strengthening through bilateral contacts with the aim of mutual acceptance of alternative methods.” A recent example for this cooperation is the active participation of US regulators at the EPAA Conference on Alternative Approaches to Animal Testing on 7 November 2005 in Brussels, organized by Vice President of the European Commission Günter Verheugen and Commissioner Janez Potočnik.

In 2003, the Commission and the US Food and Drug Administration (FDA) agreed on cooperation in cosmetics regulation for the validation of alternative test methods. In this cooperation agreement it was agreed to aim at

- co-operation and early exchange of information on the validation of test methods so as to facilitate mutual recognition, acceptance, and implementation of scientifically validated testing methods and
- joint efforts to facilitate the OECD process in providing harmonized protocols to the scientific community and promoting international adoption of validated alternative methods.

In the scientific field, since 1995, ECVAM co-operates with the US Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) with a view to an early exchange of information on the validation of test methods so as to facilitate mutual recognition, acceptance, and implementation of scientifically validated testing methods; and at joint efforts to facilitate the OECD process in providing harmonised protocols to the scientific community and promoting international adoption of validated alternative methods.

This cooperation was extended to the Japanese Centre for the Validation of Alternative Methods (“JACVAM”) which was founded in December 2005. Already now, ICCVAM, JACVAM and ECVAM are discussing the creation of an International Council of Validation Bodies, in order to harmonize procedures and collaborate strategically with OECD.

V. CONCLUSIONS

According to the information from Member States received for the present report, it can be doubted whether all Member States have established mechanisms which provide for accurate

animal testing data and effective monitoring of the application of the testing and marketing bans.

The European Commission is currently working on guidelines in order to facilitate accurate generation and collation of animal testing data relating to cosmetic products for the next annual report.

There are currently four alternative in vitro methods in relation to two toxicological endpoints (skin corrosion and acute phototoxicity) listed in Annex V of Directive 67/548/EEC. These alternative test methods are currently the only legally accepted tests at Community level aiming at fully replacing animal tests for toxicological endpoints in the area of chemicals and cosmetic products. However, concerted activities on the development and validation of alternative approaches seem promising for meeting the 2009 deadline provided by Art. 4 a of the Cosmetics Directive. 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 different levels.