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REPORT FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on the development, validation and legal acceptance of methods alternative to animal testing in the field of cosmetics (2013-2015)

1. INTRODUCTION

This is the eleventh Commission report on the development, validation and legal acceptance of methods alternative to animal testing in the field of cosmetics.

Under Article 35 of Regulation (EC) 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products[1] (the Cosmetics Regulation), each report must include information on:

- progress made in the development, validation and acceptance of methods alternative to animal testing;
- the Commission's progress on obtaining the OECD's acceptance of the alternative methods validated at EU level;
- progress on third-country recognition of the results of safety tests carried out in the EU using alternative methods;
- the specific needs of small and medium-sized enterprises (SMEs).

This report also informs the European Parliament and the Council of compliance with the deadlines for the bans set out in Article 18(1) and of related technical difficulties, pursuant to Article 18(2) of the Cosmetics Regulation.

Under Article 18(2) of the Cosmetics Regulation, the report should also cover any derogations to Article 18(1) granted in accordance with Article 18(2) of the Cosmetics Regulation. However, to date there have been no derogations granted under this provision.

After the animal testing bans became fully applicable on 11 March 2013, the report does not anymore contain statistical data on the number and type of animal experiments carried out in relation to cosmetic products in the EU (as stated in the *Communication from the Commission to the European Parliament and the Council on the animal testing and marketing ban and on the state of play in relation to alternative methods in the field of cosmetics*[2] of 11 March 2013).

The part of the report on compliance with the testing and marketing bans and the impact of the bans is based on contributions from the Member States, covering the year 2013 or 2013-2014, depending on the Member State. The part on the progress made in the development, validation and legal acceptance of alternative methods is largely based on the latest *EURL ECVAM*[3] *Status Report on the Development, Validation and Regulatory Acceptance of Alternative Methods and Approaches (2015)*[4] (2015 EURL ECVAM Status Report) which covers the period from May 2014 to September 2015. There were delays in receiving contributions from some Member States, which explains the timespan of the report.

[1] OJ L 342, 22.12.2009, p. 59.
[2] COM(2013) 135 final.
[3] European Union Reference Laboratory for Alternatives to Animal Testing, Directorate General Joint Research Centre of the European Commission, previously Institute for Health and Consumer Protection, currently Directorate F – Health, Consumers and Reference Materials.
[4] http://bookshop.europa.eu/en/eurl-ecvam-status-report-on-the-development-validation-and-regulatory-acceptance-of-alternative-methods-and-approaches-2015--pbLBNA27474/.

2. BACKGROUND

The animal testing of finished cosmetic products has been prohibited in the EU since 2004, and the testing of cosmetic ingredients since March 2009 (testing ban). Since 11 March 2009, the marketing in the EU of cosmetic products and their ingredients which have been tested on animals in order to meet the requirements of Directive 76/768/EEC[5] has also been prohibited (2009 marketing ban). This marketing ban applied to all but the most complex human health effects (endpoints) that needed to be tested to demonstrate the safety of cosmetic products in the absence of alternative non-animal tests (repeated-dose toxicity, reproductive toxicity and toxicokinetics); the European Parliament and the Council decided that the ban would take effect on 11 March 2013 (2013 marketing ban). On 11 March 2013, the Commission adopted a *Communication on the animal testing and marketing ban and on the state of play in relation to alternative methods in the field of cosmetics*. This Communication confirmed the Commission's commitment to maintaining the 2013 deadline. Therefore, the marketing ban became fully applicable as of 11 March 2013, irrespective of the availability of alternative non-animal tests.[6]

3. COMPLIANCE WITH THE TESTING AND MARKETING BANS AND THE IMPACT OF THE BANS

In practice, the main way of verifying compliance with the testing and marketing bans is the cosmetic product's product information file. Under Article 11(1) of the Cosmetics Regulation, the responsible person[7] must keep a product information file for every cosmetic placed on the EU market.

The product information file must include:

- the cosmetic product safety report referred to in Article 10(1);
- 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.[8]

In the Communication of 11 March 2013, the Commission provided guidance on information which should be included in the product information file to make it possible to verify whether animal testing was carried out in order to meet the requirements of the Cosmetics Regulation or for other purposes. The file should contain documentation on any use of the substance in products other than cosmetic products such as product examples or market data and documentation on compliance with other regulatory frameworks (e.g. the REACH Regulation[9]) and a justification of the need for the animal testing under that framework.

[5] Council Directive of 27 July 1976 on the approximation of the laws of the Member States relating to cosmetic products (76/768/EEC), OJ L 262, 27.9.1976, p. 169, repealed by the Cosmetics Regulation.
[6] A case on the interpretation of the marketing ban as laid down in Article 18(1)(b) of the Cosmetics Regulation is currently pending before the Court of Justice of the European Union (C-592/14).
[7] As defined in Article 4 of the Cosmetics Regulation.
[8] Article 11(2)(b) and (e) of the Cosmetics Regulation.
[9] 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

3.1. Inspections and compliance

Monitoring activities and checks related to compliance with the testing and marketing bans were mostly carried out in the course of regular inspections on cosmetic products, or as part of general inspections or inspection programmes targeted at specific topics or risks. No inspection programmes were *specifically* carried out to monitor compliance with the testing and marketing bans. Compliance was usually verified through checks of cosmetic products' product information files made by competent national authorities.

Four Member States reported not to have monitored compliance with the bans. This was due mostly to the specificity of the market, where cosmetic products originated mainly in other EU Member States and where local production was very limited.

During inspections carried out by market surveillance authorities, almost none of the Member States monitoring compliance detected any infringements of the testing and marketing bans.

There was one case of non-compliance with the bans reported, for a cosmetic product imported from a third country. The importer had to withdraw the product from the market, and was prosecuted and fined.

3.2. Difficulties encountered with monitoring the ban and suggestions to improve the situation

From the 23 Member States who had monitored the compliance of cosmetic products with the testing and marketing bans, a dozen did not encounter any difficulties in carrying out the checks.

The main difficulty raised by most of the remaining Member States was the fact that product information files were incomplete with regard to data on animal testing, yet this information is necessary to verify compliance with the bans.

In particular, the toxicological data (including animal testing data) on ingredients was insufficient. Moreover, the product information files did not always contain complete data on compliance with legislative frameworks other than the Cosmetics Regulation (e.g. the REACH Regulation). The information relating to animal testing was in certain cases limited to a disclaimer by the responsible person that no animal testing had been performed on the final product. In addition, it was found that some small companies have an insufficient understanding of the bans or even misinterpret their requirements.

In certain cases, the incomplete animal testing data could be explained by the fact that the suppliers of cosmetic ingredients did not provide sufficient toxicological and animal testing data to the cosmetic product manufacturer or responsible person. Responsible persons cannot always access this information if it is not provided, as it is the ingredient suppliers who commission tests.

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, 30.12.2006, p. 1.

In future reports, the issue of incomplete animal testing data in the product information file should be followed closely by competent national authorities to see how it evolves.

As reported by four Member States, there were difficulties particularly with cosmetics imported into the EU from third countries where animal tests are still required. In some of these cases, the information on animal testing was simply missing from the product information file. Two of these Member States questioned the reliability of the animal testing data received (in particular statements that no animal testing had been performed).

Two other Member States raised doubts about the joint application of the Cosmetics Regulation and the REACH Regulation. In particular, there was uncertainty about whether animal testing data should be kept for ingredients which are also used in other applications where animal testing is required under the REACH Regulation.

One Member State reported that it was not always possible to conduct checks of the product information files onsite given their size and that in these cases the responsible persons were not always willing to submit product information files to the national authority. Two Member States raised the issue of market surveillance of cosmetic products for which the responsible person is established in another Member State, in which case the authority has no direct access to the product information file.[10]

Several Member States took action to improve operators' understanding of the bans' requirements by communicating on the requirements to industry representatives. They disseminated information on the bans to economic operators through various media.[11]

3.3. Ban-related issues encountered by manufacturers, in particular SMEs, and the bans' impact on the innovativeness of the cosmetics sector

Most Member States did not report[12] any cases where a manufacturer, in particular an SME, was not able to place a cosmetic product on the market due to an inconclusive safety assessment of the product or ingredient caused by a lack of alternatives to animal testing.[13] However, one Member State pointed out that SMEs do not have the financial resources needed for cost-intensive toxicological tests on new products.

[10] However, Article 30 of the Cosmetics Regulation makes it possible for the competent authority of any Member State where the cosmetic product is made available to request the competent authority of the Member State where the product information file is made readily accessible to verify whether the product information file satisfies the requirements of Article 11(2) and whether the information set out in it provides evidence of the safety of the cosmetic product.

[11] To help address some of the issues described above, one of these Member States suggested developing a common platform to exchange information within the framework of the PEMSAC, the Platform of European Market Surveillance Authorities for Cosmetics. However, no Member State proposed to include the topic in the PEMSAC Work Programme for 2016-2017.

[12] Among these Member States, some explicitly stated that no such cases had been encountered; the others did not specifically address this question.

[13] This issue was, however, raised by one Member State. According to information received by this Member State from industry associations, it has become impossible to place certain cosmetic products on the market because the safety assessment of the product or one of its ingredients was not conclusive. It was, however, not always possible to say with certainty whether this was a direct result of the testing and marketing bans.

On the question of how the testing and marketing bans have affected the innovativeness of the cosmetics sector, most Member States either did not provide any information or reported that such information was not available to them. Views varied among the remaining nine Member States.

Four Member States were of the view that the bans had no negative impact on innovativeness. The main reason put forward was that there was already a considerable amount of animal testing data available, as well as animal testing data obtained in relation with other legislative frameworks on chemicals. These views were not always based on data and market information.

The remaining five Member States claimed that the bans may have a negative impact on innovativeness to some extent because the current level of methods alternative to animal testing does not make it possible to fully replace *in vivo* tests for all toxicological endpoints and because the bans may restrict the data available for the safety assessment of products or make it difficult to place new cosmetic ingredients on the market. These views were not always based on data and market information.

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

Significant progress was made in recent years in the development, validation and regulatory acceptance of alternative methods to test for skin irritation/corrosion, serious eye damage/eye irritation and skin sensitisation.

For skin irritation/corrosion, the regulatory accepted alternative methods now make it possible to generate data that is adequate for the classification and risk assessment of most substances. For serious eye damage/eye irritation, there is also a set of regulatory accepted alternative methods, which will in most cases be sufficient to obtain information that is adequate for classification and risk assessment. For skin sensitisation, several *in vitro/in chemico* testing methods have been validated and some have already obtained regulatory acceptance.

Despite significant progress in the development of alternative approaches, considerable scientific challenges remain for the more complex endpoints for which more research is needed.

Moreover, Directive 2010/63/EU on the protection of animals used for scientific purposes[14] which took effect in 2013 requires the Commission and the Member States to contribute to the development and validation of alternative approaches, whereas Directive 86/609/EEC only provided for their promotion.[15]

4.1. Progress in the EU

[14] Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes, OJ L 276, 20.10.2010, p. 33.

[15] 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, OJ L 358, 18.12.1986, p. 1.

4.1.1. Research and development activities

Major research and development activities on alternatives to animal testing are ongoing in the EU. More than €250 million were dedicated during the Seventh Framework Programme (FP7: 2007-2013), including from the Innovative Medicines Initiative (IMI), to research into alternatives. The five-year SEURAT-1 research initiative, which was completed in 2015, was a unique €50 million public-private partnership co-financed by the Commission's FP7 (Health Programme) and Cosmetics Europe, the European personal care association. It consisted of six individual research projects and one coordination action, and combined the research efforts of over 70 European universities, public research institutes and companies. The project's achievements were presented at the final SEURAT-1 symposium on 4 December 2015 in Brussels.[16]

As a follow-up to SEURAT-1, the EU-ToxRisk project,[17] *An Integrated European 'Flagship' Programme Driving Mechanism-based Toxicity Testing and Risk Assessment for the 21st Century*, was launched in January 2016. It is a large €30 million collaborative project funded under the Horizon 2020 programme, and involves academia, SMEs, large industry and regulatory bodies. It aims to achieve a paradigm shift in toxicology, towards a more efficient and animal-free chemical safety assessment, in particular in the field of repeated dose and developmental/reproductive toxicity testing.

There have also been other projects at European level, including the CALEIDOS project[18] that was funded under the Life+ programme from January 2013 to June 2015.[19]

4.1.2. Validation and regulatory acceptance of alternative methods

An overview of the progress of alternative methods from proposal for validation to its final adoption and inclusion into the regulatory framework will be available through a revised version of the Tracking System for Alternative test methods towards Regulatory Acceptance (TSAR).[20]

4.1.2.1. EURL ECVAM[21] activities[22]

EURL ECVAM has continued to fulfil its mandate laid down in Article 48 and Annex VII of Directive 2010/63/EU, including the validation of alternative test methods at EU level and the promotion of their regulatory acceptance.

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[16] http://www.seurat-1.eu/.
[17] http://www.eu-toxrisk.eu/.
[18] Chemical assessment according to legislation enhancing the *In silico* documentation and safe use, http://www.caleidos-life.eu/.
[19] The project explored the regulatory applicability of so-called non-testing methods (quantitative structure-activity relationship (QSAR) and read-across) to substances registered under the REACH Regulation.
[20] The revised TSAR will also cover the needs of the individual partners of EURL ECVAM participating in the International Cooperation on Alternative Test Methods (ICATM); please see section 4.2.2.
[21] European Union Reference Laboratory for Alternatives to Animal Testing, Directorate General Joint Research Centre of the European Commission.
[22] https://eurl-ecvam.jrc.ec.europa.eu/.

During the period covered by the 2015 EURL ECVAM Status Report (May 2014 to September 2015), EURL ECVAM evaluated thirty test submissions[23] and successfully carried out several validation studies. In addition, the EURL ECVAM Scientific Advisory Committee peer reviewed validation studies and issued opinions on test methods in the fields of skin sensitisation, eye and skin irritation and toxicokinetics.

EURL ECVAM published a recommendation on a successfully validated skin sensitisation test and produced a report for the OECD on the development of a test guideline on this method.[24] Two additional recommendations are currently being prepared.

More details on these activities can be found in the 2015 EURL ECVAM Status Report.

Set-up of the EU-NETVAL

In 2013, EURL ECVAM set up the EU-NETVAL,[25] the European Union Network of Laboratories for the Validation of Alternative Methods, based on Article 47(2) of Directive 2010/63/EU. EU-NETVAL's mission is to provide support primarily for EURL ECVAM validation studies. Following the 2015 call for membership, the network comprises more than thirty-five test facilities.

4.1.2.2. Regulatory uptake

Commission Regulation (EC) 440/2008[26], which brings together all regulatory accepted testing methods at EU level,[27] has been updated three times since 2013. Another update is underway.

The *in vivo* tests for skin irritation/corrosion, serious eye damage/eye irritation and skin sensitisation required under the REACH Regulation did not adequately reflect the state of science any more. Therefore, in late 2014 the Commission proposed to amend Annex VIII to the REACH Regulation to fully replace *in vivo* with *in vitro* testing for these endpoints for substances in the applicability domain of the available *in vitro* tests. The annex amendment concerning skin irritation/corrosion and serious eye damage/eye irritation was adopted on 31 May 2016[28]. The Commission proposal on skin sensitisation received a favourable vote of the REACH Committee in April 2016.

[23] Not all test methods submitted would necessarily be relevant for carrying out safety assessments of cosmetic products.
[24] For activities at OECD level, please see section 4.2.1. of this report.
[25] https://eurl-ecvam.jrc.ec.europa.eu/eu-netval.
[26] Commission Regulation (EC) No 440/2008 of 30 May 2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), OJ L 142, 31.5.2008, p. 1.
[27] Annex VIII to the Cosmetics Regulation ('List of validated alternative methods to animal testing') must be updated with alternative methods validated by ECVAM, which are not listed in Commission Regulation (EC) No 440/2008.
[28] Commission Regulation (EU) 2016/863 of 31 May 2016 amending Annexes VII and VIII to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards skin corrosion/irritation, serious eye damage/eye irritation and acute toxicity, OJ L 144, 1.6.2016, p. 27.

4.1.2.3. The European Partnership for Alternative Approaches to Animal Testing

The Commission and industry representatives together facilitate the regulatory acceptance of alternative methods and approaches under the European Partnership for Alternative Approaches to Animal Testing (EPAA). They do so by running projects, and organising and financially supporting workshops and conferences.[29]

4.1.3. Alternative methods for assessing the safety of cosmetic ingredients

The Scientific Committee on Consumer Safety (SCCS), in charge of evaluating the safety of cosmetic ingredients, recently published the 9th revision of its Notes of Guidance, with a special focus on the latest developments in the field of alternative methods and their suitability for each endpoint of the safety assessment.[30]

4.1.4. Other activities in the area of alternatives to animal testing

The topic of alternatives to animal testing, and more generally of animal welfare, has recently received considerable attention in the EU. 1.17 million citizens signed the 2015 Citizens' Initiative 'Stop Vivisection'[31] which requested to end all animal experimentation. In reply to this initiative, in its Communication of 3 June 2015[32] the Commission committed to several actions to accelerate the development and uptake of non-animal approaches in research and testing. One of these is to organise, by the end of 2016, a conference[33] engaging the scientific community and relevant stakeholders in a debate on how to exploit the advances in science for the development of scientifically valid non-animal approaches and advance towards the goal of phasing out animal testing without compromising human safety.

4.2. Progress at international level

4.2.1. Activities at OECD level

The methods for which OECD test guidelines are adopted are legally implemented at EU level through Commission Regulation (EC) 440/2008.[34] In addition, OECD-accepted methods are also suitable for regulatory use in the EU prior to their official inclusion in the Commission Regulation (EC) 440/2008.

In 2015, the Working Group of National Coordinators of the OECD test guideline programme (TGP) approved six new test guidelines, of which four were based on *in vitro* methods (on serious eye damage/eye irritation and endocrine disruption). In addition, ten existing test guidelines were updated.

[29] EPAA 2015 Annual Report, see: https://circabc.europa.eu/sd/a/54e9ad8e-0f49-4ed0-b581-36fe6e136ce4/ar-2015.pdf.
[30] http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_190.pdf.
[31] http://ec.europa.eu/citizens-initiative/public/initiatives/successful/details/2012/000007.
[32] C(2015) 3773 final.
[33] Planned for December 2016.
[34] See section 4.1.2.2. of this report.

A summary of the status of the adoption in the OECD TGP (2012-2015) of test guidelines based on alternative methods can be found in Annex I to the 2015 EURL ECVAM Status Report.

The Commission, through EURL ECVAM, plays an active role at OECD level. Within the OECD TGP, EURL ECVAM leads or co-leads ten projects on the development of new test guidelines or guidance documents.

Moreover, within the OECD Task Force on Hazard Assessment, EURL ECVAM leads projects related to the integrated approach to testing and assessment (IATA) which has become a priority over recent years as an alternative solution to animal testing. EURL ECVAM also co-chairs a group with the US Environmental Protection Agency.[35]

4.2.2. Other cooperation with third countries

At international level, the Commission is involved in various cooperation projects, notably through EURL ECVAM. These include the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, the World Health Organisation International Programme on Chemical Safety and the International Cooperation on Alternative Test Methods (ICATM)[36] set up in 2009 by the International Cooperation on Cosmetics Regulation (ICCR).[37]

ICATM members agreed to strengthen their cooperation on conducting validation studies of test methods on a voluntary basis and to create guidance on how validation studies should be conducted. An overview of the status of the validation of alternative test methods and regulatory acceptance by ICATM members can be found in Annex II to the 2015 EURL ECVAM Status Report.

The ICCR includes various projects relating to alternatives to animal testing.[38] At the ICCR ninth annual meeting held in Brussels (Belgium) from 4 to 6 November 2015, ICCR members decided to merge the different groups dealing with alternative testing methods into a working group on safety assessment methods. The group is to have a broader focus on integrated methods and approaches to the safety assessment of ingredients used in cosmetic products.

5. CONCLUSION

It has been possible to prepare the present report only in 2016, as it has been based on the contributions received from Member States between 2014 and end 2015.

[35] The OECD Extended Advisory Group on Molecular Screening and Toxicogenomics and its Adverse Outcome Pathways Development Programme.
[36] ICATM members are agencies from the EU, the United States, Japan, Canada and South Korea.
[37] ICCR is a voluntary international group of cosmetics regulatory authorities from Brazil, Canada, the EU, Japan and the United States.
[38] The ICCR working group on *In silico*/ QSAR Models produced a report on *In Silico* Approaches for Safety Assessment of Cosmetic Ingredients in July 2014: http://www.iccrnet.org/files/5314/1407/7607/2014-07_In-silico_Approaches_for_Cosmetic_Product_Safety_Assessments.pdf.

Virtually no cases of non-compliance with the testing and marketing bans have been reported by the Member States. The main issue encountered in their market surveillance activities related to the bans is the presence of cases of incomplete animal testing data in product information files.

However, this report covers the relatively early stages of the implementation of the 2013 marketing ban. It will be interesting to follow future developments in this field, when economic operators and market surveillance authorities gain more experience regarding the implementation of the full marketing ban. In particular, the issue of cases of incomplete animal testing data in the product information file should be monitored by the competent national authorities, as the product information file is the main way to verify compliance with the testing and marketing bans.

Considerable progress has been made in the development, validation and legal acceptance of methods alternative to animal testing. Nevertheless, some challenges remain for the most complex endpoints where more research is needed. The current level of alternative methods does not make it possible to fully replace *in vivo* tests for all toxicological endpoints.

Significant investments have been made in the development of alternative methods in the EU, notably through major research initiatives bringing together public and private players. The European Commission has remained engaged in the validation of alternative methods through EURL ECVAM, and in the promotion of their regulatory acceptance at OECD level and internationally.