COMMISSION REGULATION (EU) 2016/1688

of 20 September 2016

amending Annex VII 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 sensitisation

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to 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 ([1]), and in particular Articles 13(2) and 131 thereof,

Whereas:

(1) Regulation (EC) No 1907/2006 establishes requirements for the registration of substances manufactured or imported in the Union on their own, in mixtures or articles. The registrants have to provide the information required by Regulation (EC) No 1907/2006, as appropriate, in order to fulfil the registration requirements.

(2) Article 13(2) of Regulation (EC) No 1907/2006 provides that test methods used to generate information on intrinsic properties of substances required by that Regulation are to be regularly reviewed and improved with a view to reducing testing on vertebrate animals and the number of animals involved. When appropriate validated test methods become available, the Commission Regulation (EC) No 440/2008 ([2]) and the Annexes to Regulation (EC) No 1907/2006 should be amended, if relevant, so as to replace, reduce or refine animal testing. The principles of replacement, reduction and refinement, enshrined in Directive 2010/63/EU of the European Parliament and of the Council ([3]) should be taken into account.

(3) Pursuant to Regulation (EC) No 1907/2006, *in vivo* studies are required for the generation of information on skin sensitisation in point 8.3 of Annex VII to Regulation (EC) No 1907/2006.

(4) In recent years, significant scientific progress has been made in the development of alternative test methods for skin sensitisation. Several *in chemico*/*in vitro* test methods have been validated by the European Union Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM) and/or internationally agreed by the Organisation for Economic Cooperation and Development (OECD). These test methods may allow the generation of adequate information to assess whether a substance causes skin sensitisation without the need to resort to *in vivo* testing, when applied in an appropriate combination in the framework of an integrated approach to testing and assessment (IATA).

(5) To reduce animal testing, point 8.3 of Annex VII to Regulation (EC) No 1907/2006 should be amended to allow the use of these alternative methods, where adequate information can be obtained through this approach and where the available test methods are applicable for the substance to be tested.

(6) The currently available alternative test methods agreed by OECD are based on an adverse outcome pathway (AOP) describing the mechanistic knowledge about the development of skin sensitisation. These methods are not intended to be used on their own, but to be applied in combination. For the comprehensive assessment of skin sensitisation, typically methods addressing the first three key events of the AOP should be used.

([1]) OJ L 396, 30.12.2006, p. 1.
([2]) 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).
([3]) 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).

(7) However, under certain conditions, it may be possible to derive sufficient information without explicitly addressing all three key events by separate test methods. Therefore, the possibility should be given to registrants to scientifically justify the omission of tests addressing certain key events.

(8) The test method indicated as the first choice for *in vivo* testing, the local lymph node assay (LLNA), provides information on the strength of the sensitisation potential of a substance. The identification of strong skin sensitisers is important to allow appropriate classification and risk assessment of such substances. It therefore should be clarified that the requirement for information allowing an assessment whether a substance should be presumed to be a strong sensitiser applies to all data, irrespective whether they are generated *in vivo* or *in vitro*.

(9) However, in order to avoid animal testing and the repetition of already performed tests, existing *in vivo* skin sensitisation studies performed according to valid OECD test guidelines or EU test methods and in compliance to good laboratory practice ([1]) should be considered valid to fulfil the standard information requirement for skin sensitisation, even if the information derived from them is not sufficient for a conclusion whether a substance can be presumed to be a strong sensitiser.

(10) In addition, the standard information requirements and adaptation rules in 8.3 of Annex VII should be revised in order to remove redundancies with rules set by Annex VI and Annex XI and in the introductory parts of Annex VII as regards the review of available data, the waiving of studies for a toxicological endpoint if the available information indicates that the substance meets the criteria for classification for that toxicological endpoint, or to clarify the intended meaning as regards the waiving of studies for substances that are flammable under certain conditions. Where reference is made to the classification of substances, adaptation rules should be updated to reflect the terminology used in Regulation (EC) No 1272/2008 of the European Parliament and of the Council ([2]).

(11) ECHA, in cooperation with Member States and stakeholders, should further develop guidance documents for the application of the test methods and waiving possibilities for the standard information requirements provided by this Regulation for the purposes of Regulation (EC) No 1907/2006. In doing so, ECHA should take full account of the work carried out in OECD, as well as in other relevant scientific and expert groups.

(12) Regulation (EC) No 1907/2006 should therefore be amended accordingly.

(13) The measures provided for in this Regulation are in accordance with the opinion of the Committee established under Article 133 of Regulation (EC) No 1907/2006,

HAS ADOPTED THIS REGULATION:

Article 1

Annex VII to Regulation (EC) No 1907/2006 is amended in accordance with the Annex to this Regulation.

Article 2

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

([1]) Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances (OJ L 50, 20.2.2004, p. 44).

([2]) Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (OJ L 353, 31.12.2008, p. 1).

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 20 September 2016.

For the Commission
The President
Jean-Claude JUNCKER

ANNEX

Point 8.3 of Annex VII of Regulation (EC) No 1907/2006 shall be replaced by the following:

'8.3. Skin sensitisation Information allowing: — a conclusion whether the substance is a skin sensitiser and whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A), and — risk assessment, where required.	The study(ies) under point 8.3.1 and 8.3.2 do not need to be conducted if: — the substance is classified as skin corrosion (Category 1), or — the substance is a strong acid (pH ≤ 2,0) or base (pH ≥ 11,5), or — the substance is spontaneously flammable in air or in contact with water or moisture at room temperature.
8.3.1. Skin sensitisation, *in vitro/in chemico* Information from *in vitro/in chemico* test method(s) recognised according to Article 13(3), addressing each of the following key events of skin sensitisation: (a) molecular interaction with skin proteins; (b) inflammatory response in keratinocytes; (c) activation of dendritic cells.	The(se) test(s) do not need to be conducted if — an *in vivo* study according to point 8.3.2 is available, or — the available *in vitro/in chemico* test methods are not applicable for the substance or are not adequate for classification and risk assessment according to point 8.3. If information from test method(s) addressing one or two of the key events in column 1 already allows classification and risk assessment according to point 8.3, studies addressing the other key event(s) need not be conducted.
8.3.2. Skin sensitisation, *in vivo*	An *in vivo* study shall be conducted only if *in vitro/in chemico* test methods described under point 8.3.1 are not applicable, or the results obtained from those studies are not adequate for classification and risk assessment according to point 8.3. The murine local lymph node assay (LLNA) is the first-choice method for *in vivo* testing. Only in exceptional circumstances should another test be used. Justification for the use of another *in vivo* test shall be provided. *In vivo* skin sensitisation studies that were carried out or initiated before 11 October 2016, and that meet the requirements set out in Article 13(3), first subparagraph, and Article 13(4) shall be considered appropriate to address this standard information requirement.'