[X1ANNEX I

GENERAL PROVISIONS FOR ASSESSING SUBSTANCES AND PREPARING CHEMICAL SAFETY REPORTS

Editorial Information

X1 Substituted by Corrigendum 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 (Official Journal of the European Union L 396 of 30 December 2006).

1. HUMAN HEALTH HAZARD ASSESSMENT

1.0. Introduction

[F1 1.0.1. The objectives of the human health hazard assessment shall be to determine the classification of a substance in accordance with Regulation (EC) No 1272/2008; and to derive levels of exposure to the substance above which humans should not be exposed. This level of exposure is known as the Derived No-Effect Level (DNEL).]

Textual Amendments

F1 Substituted by Commission Regulation (EU) No 252/2011 of 15 March 2011 amending 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 Annex I (Text with EEA relevance).

[F1 1.0.2. The human health hazard assessment shall consider the toxicokinetic profile (i.e. absorption, metabolism, distribution and elimination) of the substance and the following groups of effects:

(1) acute effects such as acute toxicity, irritation and corrosivity;

(2) sensitisation;

(3) repeated dose toxicity; and

(4) CMR effects (carcinogenity, germ cell mutagenicity and toxicity for reproduction).

Based on all the available information, other effects shall be considered when necessary.]

1.0.3. The hazard assessment shall comprise the following four steps:

Step 1 : Evaluation of non-human information.
Step 2 : Evaluation of human information.
Step 3 : Classification and Labelling.
Step 4 : Derivation of DNELs.

[F2 The assessment shall address all nanoforms that are covered by the registration.]

Textual Amendments

F2 Inserted by Commission Regulation (EU) 2018/1881 of 3 December 2018 amending 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 Annexes I, III,VI, VII, VIII, IX, X, XI, and XII to address nanoforms of substances (Text with EEA relevance).

1.0.4. The first three steps shall be undertaken for every effect for which information is available and shall be recorded under the relevant section of the Chemical Safety Report and where required and in accordance with Article 31, summarised in the Safety Data Sheet under headings 2 and 11.

1.0.5. For any effect for which no relevant information is available, the relevant section shall contain the sentence: 'This information is not available'. The justification, including reference to any literature search carried out, shall be included in the technical dossier.

1.0.6. Step 4 of the human health hazard assessment shall be undertaken by integrating the results from the first three steps and shall be included under the relevant heading of the Chemical Safety Report and summarised in the Safety Data Sheet under heading 8.1.

1.1. Step 1: Evaluation of non-human information

1.1.1. The evaluation of non-human information shall comprise:

— the hazard identification for the effect based on all available non-human information,

— the establishment of the quantitative dose (concentration)-response (effect) relationship.

1.1.2. When it is not possible to establish the quantitative dose (concentration)-response (effect) relationship, then this should be justified and a semi-quantitative or qualitative analysis shall be included. For instance, for acute effects it is usually not possible to establish the quantitative dose (concentration)-response (effect) relationship on the basis of the results of a test conducted in accordance with test methods laid down in a Commission Regulation as specified in Article 13(3). In such cases it suffices to determine whether and to which degree the substance has an inherent capacity to cause the effect.

[[F1]1.1.3. All non-human information used to assess a particular effect on humans and to establish the dose (concentration) – response (effect) relationship, shall be briefly presented, if possible in the form of a table or tables, distinguishing between *in vitro*, *in vivo* and other information. The relevant test results (e.g. ATE, LD50, NO(A)EL or LO(A)EL) and test conditions (e.g. test duration, route of administration) and other relevant information shall be presented, in internationally recognised units of measurement for that effect.**]**

1.1.4. If one study is available then a robust study summary should be prepared for that study. If there are several studies addressing the same effect, then, having taken into account possible variables (e.g. conduct, adequacy, relevance of test species, quality of results, etc.), normally the study or studies giving rise to the highest concern shall be used to establish the DNELs and a robust study summary shall be prepared for that study or studies and included as part of the technical dossier. Robust summaries will be required of all key data used in the hazard assessment. If the study or studies giving rise to the highest concern are not used, then this shall be fully justified and included as part of the technical dossier, not only for the study being used but also for all studies demonstrating a higher concern than the study being used. It is important

irrespective of whether hazards have been identified or not that the validity of the study be considered.

1.2. Step 2: Evaluation of human information

If no human information is available, this part shall contain the statement: 'No human information is available'. However, if human information is available, it shall be presented, if possible in the form of a table.

1.3. Step 3: Classification and Labelling

[F1 1.3.1. The appropriate classification developed in accordance with the criteria in Regulation (EC) No 1272/2008 shall be presented and justified. Where applicable, Specific Concentration limits resulting from the application of Article 10 of Regulation (EC) No 1272/2008 and Articles 4 to 7 of Directive 1999/45/EC shall be presented and, if they are not included in Part 3 of Annex VI to Regulation (EC) No 1272/2008, justified.

[F3 The assessment should always include a statement as to whether the substance or, when applicable, nanoforms thereof fulfils or does not fulfil the criteria given in Regulation (EC) No 1272/2008 for classification in the hazard class carcinogenicity category 1A or 1B, in the hazard class germ cell mutagenicity category 1A or 1B or in the hazard class reproductive toxicity category 1A or 1B.**]**

Textual Amendments

F3 Substituted by Commission Regulation (EU) 2018/1881 of 3 December 2018 amending 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 Annexes I, III,VI, VII, VIII, IX, X, XI, and XII to address nanoforms of substances (Text with EEA relevance).

[F3 1.3.2. If the information is inadequate to decide whether a substance or, when applicable, nanoforms thereof should be classified for a particular hazard class or category, the registrants shall indicate and justify the action or decision he has taken as a result.**]]**

1.4. Step 4: Identification of DNEL(s)

1.4.1. Based on the outcomes of steps 1 and 2, (a) DNEL(s) shall be established for the substance, reflecting the likely route(s), duration and frequency of exposure. **[**F1 For some hazard classes, especially germ cell mutagenicity and carcinogenicity, the available information may not enable a toxicological threshold, and therefore a DNEL, to be established.**]** If justified by the exposure scenario(s), a single DNEL may be sufficient. However, taking into account the available information and the exposure scenario(s) in Section 9 of the Chemical Safety Report it may be necessary to identify different DNELs for each relevant human population (e.g. workers, consumers and humans liable to exposure indirectly via the environment) and possibly for certain vulnerable sub-populations (e.g. children, pregnant women) and for different routes of exposure. A full justification shall be given specifying, *inter alia*, the choice of the information used, the route of exposure (oral, dermal, inhalation) and the duration and frequency of exposure to the substance for which the DNEL is valid. If more than one route of exposure is likely to occur, then a DNEL shall be established for each route of exposure and for the exposure from all routes combined. When establishing the DNEL, the following factors shall, *inter alia*, be taken into account:

(a) the uncertainty arising, among other factors, from the variability in the experimental information and from intra- and inter-species variation;

(b) the nature and severity of the effect;

(c) the sensitivity of the human (sub-)population to which the quantitative and/or qualitative information on exposure applies.

1.4.2. If it is not possible to identify a DNEL, then this shall be clearly stated and fully justified.**]**

Status:
Point in time view as at 31/01/2020.

Changes to legislation:
There are currently no known outstanding effects for the Regulation (EC) No 1907/2006 of the European Parliament and of the Council, Division 1..