



Committee of Experts on the Transport of Dangerous Goods and on the Globally Harmonized System of Classification and Labelling of Chemicals

Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals

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Item 3 (c) of the provisional agenda

Work on the Globally Harmonized System of Classification and Labelling of Chemicals: use of non-animal testing methods for classification of health hazards

Consequential amendments to chapters 1.2, 3.2 and 3.3 due to the revision of Chapter 3.4 to fully incorporate non-animal test methods for skin sensitization

Transmitted by the experts from the United Kingdom and the
Netherlands on behalf of the informal working group on the use of non-
animal test methods for classification of health environmental hazards
hazards*

Introduction

1. In documents ST/SG/AC.10/C.4/2022/14 and informal document INF.3, a revised Chapter 3.4 for the GHS to fully incorporate non-animal test methods for skin sensitization is proposed. The proposed changes to Chapter 3.4 also necessitates a number of conforming changes to be made to Chapter 1.2, Chapter 3.2 and Chapter 3.3, as outlined below in paragraphs 2 to 6.

Proposed conforming changes to Chapter 1.2

2. Amend Chapter 1.2 “Definitions and abbreviations” as follows:

Insert a new definition after the entry for “Critical temperature”, to read as follows:

“**Defined approach** means an approach to testing and assessment that consists of a fixed Data Interpretation Procedure used to interpret data generated with a defined set of information sources, that can either be used on its own, or together with other information sources within an overall weight of evidence, to satisfy a specific regulatory need;”

* A/75/6 (Sect.20), para. 20.51.

Proposed conforming changes to Chapter 3.2

Note: The amendment below supplements the amendments to Chapter 3.2 adopted by the Sub-Committee at its fortieth session (see ST/SG/AC.10/C.4/80, Annex I).

3. In 3.2.2.6 “*Classification based on non-test methods (Tier 5 in Figure 3.2.1)*”, insert the following new paragraph after 3.2.2.6.3:

“3.2.2.6.4 For conclusions on no classification from read-across and (Q)SARs the adequacy and robustness of the scientific reasoning and of the supporting evidence should be well substantiated and normally requires multiple negative substances with good structural and physical (related to toxicokinetics) similarity to the substance being classified, as well as a clear absence of positive substances with good structural and physical similarity to the substance being classified.”

Proposed conforming changes to Chapter 3.3

Note: The amendments below refer to the text of Chapter 3.3 adopted by the Sub-Committee at its fortieth session (see ST/SG/AC.10/C.4/80, Annex I).

4. In 3.3.2.3 “*Classification based on defined approaches (Tier 2 in Figure 3.3.1)*”:

- insert a new paragraph number ‘3.3.2.3.1’ at the beginning of the text for 3.3.2.3 to read as follows:

“3.3.2.3.1 Defined approaches consist of...”

- insert two new paragraphs after 3.3.2.3.1, as follows:

“3.3.2.3.2 Where the results from defined approaches are assigned a level of confidence, a low confidence outcome of a defined approach cannot be used on its own to classify but may be considered in combination with other data.

3.3.2.3.3 Some evidence can be used individually and in defined approaches. Evidence used within defined approaches should then not also be used individually within a weight of evidence assessment.”

5. In 3.3.2.4 ‘*Classification based on in vitro/ex vivo data (Tier 2 in Figure 3.3.1)*’,

- insert a new paragraph 3.3.2.4.2 after 3.3.2.4.1, to read as follows:

“3.3.2.4.2 *In vitro/ex vivo* methods in 3.3.2.4.1 with the result “no stand-alone prediction can be made” should within Tier 2 only be used in combination with other types of data in defined approaches. When already considered within a defined approach, *in vitro/ex vivo* methods should not be considered as an additional line of evidence.”

- amend current paragraph numbers for “3.3.2.4.2” to read: “3.3.2.4.3” and “3.3.2.4.3” to read: “3.3.2.4.4”

6. In 3.3.2.8 ‘*Classification based on non-test methods for serious eye damage/eye irritation or for skin corrosion (Tier 6 in Figure 3.3.1)*’:

- replace 3.3.2.8.1 with the following:

“3.3.2.8.1 Classification, including the conclusion not classified, can be based on non-test methods, with due consideration of reliability and applicability, on a case-by-case basis. Specific non-test methods may also be used in a defined approach. When already considered within a defined approach, these specific non-test methods should not be considered as an additional line of evidence. Non-test methods include computer models predicting qualitative structure-activity relationships (structural alerts, SAR) or quantitative structure-activity relationships (QSARs), computer expert systems, and read-across using analogue and category approaches.”

- Insert the following new paragraph 3.3.2.8.5:

“3.3.2.8.5 For conclusions on no classification from read-across and (Q)SARs the adequacy and robustness of the scientific reasoning and of the supporting evidence should be well substantiated and normally requires multiple negative substances with good structural and physical (related to toxicokinetics) similarity to the substance being classified, as well as a clear absence of positive substances with good structural and physical similarity to the substance being classified.”

Action and next steps

7. The Sub-Committee is invited to agree the proposed conforming changes to Chapter 1.2, Chapter 3.2 and Chapter 3.3 due to proposed changes to Chapter 3.4 for skin sensitization, as set out in paragraphs 2 to 6 of this document.
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