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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

Fortieth session
Geneva, 5-7 July 2021
Item 2 (e) of the provisional agenda
Work on the Globally Harmonized System (GHS): classification criteria for germ cell mutagenicity (sub-category 1B)

Terms of reference and work programme of the informal working group on the criteria for classification for germ cell mutagenicity

Transmitted by the European Union on behalf of the informal working group on the criteria for classification for germ cell mutagenicity*

Background

1. Reference is made to the proposal contained in ST/SG/AC.10/C.4/2020/13, informal document INF.37 (39th session) (European Union) on the *Clarification of the criteria for classification for germ cell mutagenicity in category 1B* and the report of the Sub-Committee on its thirty-ninth session (ST/SG/AC.10/C.4/78). At the 39th session, the Sub-Committee agreed in principle to the proposal to address the issue described in the informal document INF.37 within an informal working group on condition that OECD would be engaged in the work. The Sub-Committee agreed that the first task of the informal working group would be to discuss and agree on the terms of reference for its work on the basis of the draft informal document INF.37 and taking into account the comments made by the Sub-Committee, such as the discussion of any work to capture non-animal test methods with the non-animal testing informal working group. The informal working group should forward the agreed terms of reference and a detailed work programme to the Sub-Committee for its consideration at a future session. It was noted that the work of the informal working group would be organized by the Joint Research Centre (JRC) of the European Commission.

2. The draft terms of reference were discussed at the kick-off meeting of the informal working group on the criteria for classification for germ cell mutagenicity held on 2 March 2021, with the aim to submit the terms of reference proposed by the informal working group for approval at the fortieth session of the Sub-Committee together with a detailed work programme.

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

3. Although the original proposal agreed by the Sub-Committee focused on the revision of the criteria for Category 1B, members of the informal working group felt the need to also review criteria in categories 1A and 2. In particular, the criterion for Category 1A has been extremely difficult to apply due to unavailability of data from human epidemiological studies as well as limited guidance. Overall, it will be important to clarify the rigour of evidence needed to classify in each of the categories.

4. Besides the items specified in the informal document INF. 37 the following additional issues, as further detailed below, were included in the terms of reference: (i) review the criteria for classification in Category 1A and Category 2, (ii) ensure that the revised criteria are consistent with each other, and (iii) amend the decision logic and guidance in Chapter 3.5, if necessary to be in line with the revised criteria.

Proposal

5. The following terms of reference are proposed for the informal working group[1]:

(a) Review criteria for classification:

(i) Review the criteria for classification in Category 1B, including the use of other types of data as indirect evidence of interaction with germ cells; such as toxicokinetic data from currently accepted *in vivo* studies and/or supporting evidence from other available studies.

(ii) Review the criteria for classification in Category 2.

(iii) Review the criterion for classification in Category 1A.

(iv) Consider whether revisions are required to the criteria and revise the criteria, and/or provide additional guidance, as needed, in accordance with the results of the review.

(v) Ensure that the criteria are consistent with each other following any revisions.

(b) Ensure that the wording throughout the text of the chapter is coherent and not redundant and avoid the inconsistent use of the word “mutagenicity” and “heritable”.

(c) Update the chapter according to current state of science, including newly available test guidelines as appropriate. Consider whether to include non-test guideline assays and regrouping of the tests.

(d) Include paragraphs regarding non-testing methods similar to that in the newly revised Chapter 3.2 on skin corrosion/irritation and extend the note on read-across to be in line with that chapter. In addition, indicate that a read-across can be supported by positive results in *in vitro* mammalian mutagenicity assays.

(e) Prepare draft amendments and additions to the GHS to facilitate hazard classification using non-animal methods, where appropriate, and consult with the informal working group on non-animal testing methods (NATM) for submission, as a proposal in a working document directly to the Sub-Committee.

(f) Review current section 3.5.5 on decision logic and guidance in line with any revised criteria.

(g) Consider any new information relevant to the work provided by other international organizations or institutions, such as OECD or the Health and Environmental Sciences Institute (HESI).

[1] It is not foreseen to review the sections on mixtures.

(h) Identify technical errors and/or editorial improvements during the review of chapters that are not related to classification of germ cell mutagenicity and send them to the practical classification issues (PCI) informal working group for submission as a proposal in a working document directly to the Sub-Committee.

(i) Report progress to the Sub-Committee as appropriate.

Work programme

6. The work will be carried out through discussions in approximately bi-monthly meetings and by written procedure, based on the issues to discuss. The meetings will be organised on-line or as face-to-face meetings in the margins of the Sub-Committee meetings. The JRC on behalf and in agreement with the informal working group will inform the Sub-Committee on the progress of the informal working group at each Sub-Committee meeting.

7. Any new information relevant to the different issues provided by other international organizations or institutions, such as OECD or the Health and Environmental Sciences Institute (HESI), will be discussed when deemed necessary throughout the work of the informal working group.

8. The proposed workstreams are detailed below:

Workstream 1

(a) Terminology

(b) Update the chapter according to current state of science as described in (c).

(c) Non-testing methods, read-across and consulting with the informal working group on NATM.

Workstream 2: Review criteria

(a) Review and revise, as needed, the criteria for category 1B

(b) Review and revise, as needed, the criteria for category 2

(c) Review and revise, as needed, the criteria for category 1A

Workstream 3: Explore the relevant sections in Chapter 3.5 with reference to the results of workstream 1 and 2 and propose additional or modifying text, if deemed necessary

(a) Ensure that any revised criteria for the different categories are consistent with each other.

(b) Decision logic and guidance.

(c) Consult with the PCI informal working group on technical errors and/or editorial improvements.

9. The objective of the informal working group is to finalise a draft revised text of Chapter 3.5 and present to the sub-committee within this biennium and prior to December 2022 for possible inclusion in the tenth revised edition of the GHS.