

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**

11 June 2020

Thirty-ninth session

Geneva, 8-10 July 2020

Item 2 (i) of the provisional agenda

**Classification criteria and related hazard communication:
other issues**

Comments on ST/SG/AC.10/C.4/2020/13 "Clarification of the criteria for classification for germ cell mutagenicity in category 1B"

Transmitted by the expert from Germany

1. The expert from Germany wishes to thank the EU for bringing up this topic and for the work provided in document ST/SG/AC.10/C.4/2020/13. We agree that there has been development concerning mutagenicity testing and it is highly welcomed to adopt Chapter 3.5 to the technical progress made.
2. Germany therefore approves to amend the current criteria in GHS chapter 3.5. We acknowledge for example that the present requirement for “demonstrating the ability of the substance or its metabolite(s) to interact with the genetic material of germ cells” has been causing difficulties regarding category 1B classifications.
3. However, the consequences of the proposal made in ST/SG/AC.10/C.4/2020/13 need to be thoroughly evaluated. To our understanding, the proposal is modifying the criteria in a way that might be considered as extending the scope of substances classified for mutagenicity 1 B under GHS. A discussion is needed whether this is intended and whether this is consensus view in the GHS Sub-Committee.
4. Germ cell mutagenicity tests are scarce, require many animals, and often no clear results are obtained. Furthermore, they are not validated to cover all genotoxicity endpoints or genotoxic alterations in female germ cells. Progress in testing methods and the experience gained with the application of the criteria should be reflected during revision of the chapter.
5. Also, additional changes in GHS chapter 3.5 might be necessary for means of consistency. Therefore, we do support the intention of the document, however, without thorough discussion Germany does not support the proposed amendments in ST/SG/AC.10/C.4/2020/13 in the current form.

Proposal for the Sub-Committee

6. To facilitate a discussion of all relevant and necessary changes concerning chapter 3.5 and initiate a meaningful and consistent amendment the Sub-Committee is invited to consider developing an according proposal for the programme of work in the next biennium. Possibly the EU would feel in the position to take the lead of an informal working group on that aspect? The specific experts from Germany would be willing to participate and support the work.

Specific comments for discussion

Please find in the following a list of specific comments from our experts which might need to be addressed and discussed in an informal working group.

- (i) The word “heritable” is proposed to be deleted in Figure 3.5.1 As the word “heritable” was so far not proposed to be deleted in GHS section 3.5.2.5, where examples for test methods are given, this section would be left without reference to the criteria in figure 3.5.1 (a). Which test would be an example for an in vivo germ cell mutagenicity tests in mammals in case 'heritable' would be deleted in GHS figure 3.5.1 (a)? Would section 3.5.2.5 then merge with section 3.5.2.7?
- (ii) There is already a proposal by CropLife to amend the list of test examples provided in GHS 3.5.2.5 to 3.5.2.9. Further amendments might be reasonable and should be considered. For example OECD TG 488 (Transgenic Rodent Somatic and Germ Cell Gene Mutation Assays), OECD TG 489 (In Vivo Mammalian Alkaline Comet Assay), OECD TG 490 (In Vitro Mammalian Cell Gene Mutation Tests Using the Thymidine Kinase Gene), OECD TG 487 (In Vitro Mammalian Cell Micronucleus Test) might be added.
- (iii) Also it could be discussed whether ‘non-guideline’ tests (such as the Spermatid Micronucleus Assay) or tests where guidelines were deleted following an OECD Council decision (such as the Mammalian Bone Marrow Sister Chromatid Exchange Test – SCE) should be deleted from the list of as examples.
- (iv) The Bacterial reverse mutation test (OECD 471) is currently provided in GHS as an example of an in vitro mutagenicity test. The changes proposed in ST/SG/AC.10/C.4/2020/13 might lead to situations where this test (if positive) plays a much stronger role for mutagenicity 1B classification as in the actual version of the criteria. Is this really intended?
- (v) Following the proposed changes in the classification criteria, positive evidence obtained from “other in vivo somatic cell genotoxicity tests in mammals which are supported by positive results from in vitro mutagenicity assays” is given high relevance for mutagenicity 1 B classification. This seems strange compared to the fact that genotoxicity tests in germ cells in vivo are mentioned as 'supportive evidence' only.
- (vi) The proposed addition to the 'Note' (revision proposal '7d') “similarly, substances for which read-across to substances classified in category 1B is applicable, classification in 1B should be considered.” may be confusing in the light of the already existing first part of the 'NOTE' “Substances....which also show structure activity relationship to known germ cell mutagens, should be considered for classification as Category 2 mutagens”. Thus, amending the text in the ‘Note’ is suggested in order to avoid misinterpretation. The following clarification is proposed:

“Substances which are positive in in vitro mammalian mutagenicity assays, and for which read-across to substances already classified in a given germ cell mutagenicity category (1A/1B/2) is applicable, should be considered for classification in the same or lower hazard category as the source substance; i.e. for instance, substances for which read-across to substances classified in category 1B is applicable, classification in 1B or 2 should be considered.
