



**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****Thirty-first session**

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Item 3 (f) of the provisional agenda

**Classification criteria and related hazard communication:
miscellaneous****Use of non-animal testing methods for the classification of
health hazards: terms of reference for the informal working
group****Transmitted by the experts from the Netherlands and the United
Kingdom¹****Introduction**

1. The Netherlands and the United Kingdom submitted paper ST/SG/AC.10/C.4/2015/13 on the use of non-animal testing methods for the classification of health hazards, for discussion at the 30th session of the Sub-Committee.
2. Tests that determine hazardous properties, which are conducted according to internationally recognized scientific principles, can be used for purposes of a hazard determination for health and environmental hazards. Although not explicitly mentioned, it is clear that most classification criteria were originally based on animal test methods because the GHS criteria were at that time based on available (animal) data. There are several difficulties in applying alternatives to animal testing to classify substances and mixtures, especially read-across approaches and in vitro test methods.

¹ In accordance with the programme of work of the Sub-Committee for 2015–2016 approved by the Committee at its seventh session (see ST/SG/AC.10/C.4/56, annex III and ST/SG/AC.10/42, para. 15).

3. One option to avoid animal testing is to use data from relevant analogous substances using grouping approaches. Several suggestions on how to apply grouping approaches are available. For example, the OECD published a guidance document (Series on testing and assessment, number 102) on the (Q)SAR application toolbox to develop chemical categories according to the OECD guidance on grouping of chemicals. The European Chemical Agency (ECHA) recently published its “Read-Across Assessment Framework (RAAF)” that provides a structure for the scientific evaluation of grouping approaches for mono-constituent substances under REACH dossier evaluation. And in the United States of America, the Environmental Protection Agency has provided the “Analog Identification Methodology (AIM)” to facilitate analog analysis and data identification in support of chemical assessment and grouping approaches.

4. A second option to avoid animal testing is the use of in vitro test methods according to guidelines developed by OECD. The use of *in vitro* test methods for classification of substances and mixtures can be limited because the GHS does not explicitly mention criteria for the results from *in vitro* tests. Although OECD test methods are continuously developing and new *in vitro* methods will become available, it is difficult to connect the outcome of the *in vitro* test with the GHS criteria.

5. The conclusions of the discussions as recorded in the report of the 30th session (document ST/SG/AC.10/C.4/60) were as follows.

“27. There was general support for reviewing international efforts to non-animal approaches including *in vitro* and *in chemico* test methods for classification. There was also support for discussion on how to incorporate these, considering the limitations and ambiguities identified, in the use of non-animal testing methods for health hazard evaluation in accordance with the GHS.

28. The experts from the Netherlands, the United Kingdom and the United States of America volunteered to work on the terms of reference for the work to be submitted to the Sub-Committee for consideration at its next session. It was recognized that two different approaches might be needed to address the issues raised, i.e:

- evaluation of “read-across” methods; and
- evaluation of *in vitro* and *in chemico* test methods;

29. Several experts suggested that a “pilot” hazard class be selected for evaluation of the test methods and considered that once the evaluation had been completed for this hazard class, the exercise could be extended to other hazard classes.

30. The Chairman of the TDG Sub-Committee urged that the needs for transport of dangerous goods be considered during this work.”

Proposal

6. The experts from the Netherlands and the United Kingdom consider the most appropriate way forward to be the establishment of a GHS informal working group on promoting the use of non-animal test methods in GHS classification. The working group would work in a step-wise fashion, taking into account that a “one-size-fits-all” approach may not be appropriate for all hazard classes.

7. The following terms of reference are proposed for the informal working group:
- (a) Identify and evaluate², relative to existing accepted *in vivo* test methods:
 - (i) The existing guidance on grouping approaches that could be useful for GHS health hazard classification, including their limitations and uncertainties; and
 - (ii) The available *in vitro* and *in chemico* methods test methods, validated at international level, that could be used for GHS health hazard classification, including their applicability domains, limitations (such as accuracy, sensitivity, specificity) and expected future developments.
 - (b) For each relevant GHS hazard class and category, assess:
 - (i) Where substances and mixtures may be classified using grouping approaches, taking into account all relevant scientific information; and whether new or amended GHS classification criteria are needed to facilitate the use of such methods for hazard classification, and
 - (ii) Where the results of validated *in vitro* or *in chemico* test methods can be used directly for hazard classification of substances and mixtures, and whether new or amended GHS classification criteria are needed to facilitate the use of such methods for hazard classification.
 - (c) Prepare draft amendments and additions to the GHS to facilitate health hazard classification using grouping and *in vitro* or *in chemico* approaches, where appropriate and considering relevant limitations and uncertainties. The proposed changes should provide, so far as possible, a consistent approach across the different hazard classes. They should include as appropriate classification criteria, notes, decision logic, tiered evaluation and guidance, and should take into account the needs of all sectors. If appropriate, suggestions for further developments of read across and *in vitro* or *in chemico* approaches should be given.
 - (d) Report progress to the GHS Sub-Committee as appropriate.

In taking forward its work the informal working group may wish to establish sub-groups on read across and on *in vitro/in chemico* approaches. The informal working group may also want to take a stepwise approach, starting with selected hazard classes and categories.
8. The Sub-committee is invited to agree the terms of reference in paragraph 7 above for the informal working group on promoting the use of non-animal test methods in GHS classification.

² It is not foreseen to have a complete evaluation of all existing guidance or to cover all new developments. The work by the informal working group should focus on relevant information in relation the possible amendments or additions to GHS classification.