

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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DEVELOPMENT OF GUIDANCE ON THE APPLICATION OF GHS CRITERIA

Pilot program to test the classification criteria for mixtures

Transmitted by the expert from the United States of America

Purpose

1. The purpose of this information document is to provide an update on the status of the pilot program to test the mixture's rules of the GHS.

Background

2. In 2005, a pilot project was conducted between the occupational safety and health authorities in the EU and USA to classify two chemicals according to the principles of the GHS (UN/SCEGHS/10/INF.5). The two chemicals were methyl tert-butyl ether and glutaraldehyde and the purpose of the project was to better understand the application of the GHS. This 2005 pilot project was designed to address single substances, however, as glutaraldehyde is marketed in solution (generally 2%), its use resulted in extending the pilot to mixtures.
3. During the twelfth meeting of UN/SCEGHS held in December 2006, an informal group met to discuss a mixtures' pilot program. At that meeting, an exercise was provided that included information on the health hazard classifications for seven fictitious chemicals, along with the components for three mixtures of the fictitious chemicals. Group members were asked to classify the mixtures according to the provided information and the GHS mixtures' rules. The purpose of the exercise was to determine differences in approach to classification.
4. Eight work group participants submitted results. All health hazards other than aspiration hazard were evaluated. The results show that there were, indeed, inconsistencies in the application of the classification criteria for mixtures.

5. The remainder of this paper will discuss the specific issues that came out of this exercise and will also discuss additional issues for the next phase of this project. Some of the issues to be covered in the next phase of testing were a direct outcome of this exercise. Others were noted by the classifiers as areas where clarification is needed.

Results of the mixtures' pilot

(a) *Application of bridging principles*

6. Many classifiers made use of the dilution bridging principle as equivalent to the Acute Toxicity Estimate and the cut-off tables, although not all classifiers considered this to be the appropriate use of this bridging principle.
7. Clarification may be needed that the GHS presents a tiered approach which leads to a decision at each tier and that the tiers are not necessarily interchangeable. That is, if the criteria for the first tier are not available, the classifier resorts to the second tier, the bridging principles. If the criteria for the bridging principles are not met, the third tier must be employed.
8. Specifically, paragraph 1.3.2.3 Classification criteria, explains that the recommended process for classification of mixtures is based on the sequence of (1) available test data for the mixture, (2) bridging principles per the specific chapter language, and (3) the agreed method(s), as described in each chapter for estimating hazards based on the information known.
9. An example is for Acute Toxicity. In the exercise, data was provided for seven substances. No data was provided for mixtures. The introductory paragraph for the application of bridging principles for Acute Toxicity, Paragraph 3.1.3.5.1, provides the following: "Where the mixture itself has not been tested to determine its acute toxicity, but there are sufficient data on the individual ingredients and similar tested mixtures to adequately characterize the hazards of the mixture, these data will be used in accordance with the following agreed bridging principles. This ensures that the classification process uses the available data to the greatest extent possible in characterizing the hazards of the mixture without the necessity for additional testing in animals."
10. In the above paragraph, two conditions are necessary for the use of the bridging principles. The first is that there are sufficient data on the individual ingredients and the second is that there is sufficient data on similar tested mixtures to adequately characterize the hazards of the new mixture. While sufficient data was provided on individual ingredients in the exercise, no data was provided for similar tested mixtures. Therefore, the dilution bridging principle should likely not have been applied, and this raises the question of the appropriate application of this paragraph.

(b) *Clarity of terms*

11. There was inconsistency in the interpretation of the terms "No data available," "Not applicable," and "Not classified."

12. The exercise used all three terms. “Not applicable” and “Not classified” were intended to be essentially equivalent and meant that the hazard was not applicable to that chemical. “No Data” meant that the substance had not been tested for a hazard endpoint and it was unknown whether or not the substance represented that hazard.
13. Paragraph 3.1.3.6.1 provides the formula for the acute toxicity estimate (ATE) when all ingredients are of known toxicity. Paragraph 3.1.3.6.2.3 provides the formula for the ATE of a mixture when >10% of the ingredients is of unknown toxicity.
14. As there is a difference regarding which formula is to be used when the information is either known or unknown, clarification on these terms and which formula to apply would be useful. It should be noted that terms not used in this exercise might also be encountered in hazard classification. For instance, the hazard may be “unknown” or “not established.” In fact, the meaning of “not established” and “not classified” could be considered debatable. General guidance on the use of such terms and their application in the GHS may be warranted.

(c) Acute toxicity: paragraph 3.1.3.2

15. The “plain language reading” of paragraph 3.1.3.2 allows for classification of acute toxicity by one route exposure, if that route can be followed for all ingredients. The language of the paragraph follows:

Classification of mixtures for acute toxicity can be carried out for each route of exposure, but is only needed for one route of exposure as long as this route is followed (estimated or tested) for all ingredients. If the acute toxicity is determined for more than one route of exposure, the more severe hazard category will be used for classification. All available information should be considered and all relevant routes of exposure should be identified for hazard communication.

16. In the exercise, one classifier chose to determine the classification for one route only, resulting in an overall classification that was less severe than that determined by other classifiers, who evaluated the information on all routes of exposure and chose the most severe. Clarification of the application of this paragraph may be warranted, as this outcome seems counterintuitive. Additionally, clarification of the footnote to paragraph 3.1.3.6.2.1(a) and its relationship to paragraph 3.1.3.2 was requested.

(d) Serious eye damage/Eye irritation

17. The flow diagram listed as Figure 3.3.1 for serious eye damage/eye irritation, is provided in the GHS as classification criteria for substances, but was sometimes used for the classification of the untested mixtures provided in this exercise.
18. The tables and decision logic in Chapter 3.3 on serious eye damage/eye irritation needs to be reconciled. The differences between the tables and the flow diagram resulted in different categories for this hazard endpoint. Table 3.3.2, Table 3.3.5, and the decision logics on pages 147-150 include classification into Categories 2A and 2B. Tables 3.3.3 and 3.3.4 provide classification based on cut-off values, but do not sub-divide Category 2.

19. There are several possible resolutions in need of consideration. For instance, Table 3.3.3 could be revised to include Categories 1, 2A and 2B. Another resolution could be that only Category 2A is included in the table with the explanation that 2B can only be determined through test data and cannot be calculated. Other resolutions could be considered.

(e) ***Carcinogenicity, Mutagenicity, Reproductive Toxicity***

20. In each of these chapters, there is inconsistency regarding the division of categories throughout the chapters. Specifically, the sections on classification criteria for substances and the labelling elements list Categories 1A, 1B, and 2. The tables with the cut-off concentrations for mixtures and the flow diagrams only provide for Categories 1 and 2. One solution may be to clarify that the cut-off tables and flow diagrams apply to Categories 1A and 1B.

(f) ***Reproductive toxicity***

21. Guidance is needed for cases in which a mixture is both a Category 1 and Category 2 reproductive toxin. In such a situation, portions of both hazard communication elements might be necessary in that the hazard statement includes two hazard endpoints (damage to fertility and damage to the unborn child). It may be that for this hazard the most severe category will not necessarily take precedence.

(g) ***STOT – Single exposure***

22. Clarify that a Category 3 classification is an independent step from the Category 1/2 classification and that a mixture could be a Category 1 or 2 for STOT (Single exposure) AND a Category 3. In the exercise, not all classifiers included Category 3 when the more severe hazard category (Category 1 or 2) was represented.
23. Provide guidance that within a Category 3 classification, a separate assessment needs to be conducted on respiratory irritation versus narcotic effects.
24. Clarification is needed on whether the 20% concentration limit in 3.8.3.4.5 should be applied as an additive or non-additive effect. That is, whether each Category 3 ingredient (for each endpoint) should be added together and compared to the 20% level or whether each ingredient is considered separately.

Issues to be addressed in the next testing phase

- (a) Incorporate the concept of unknowns into the ATE calculation. This would provide further insight into the application of paragraphs 3.1.3.6.1 and 3.1.3.6.2.3;
- (b) Provide ingredients with data in Category 5 and above for acute toxicity (e.g., Oral data > 5,000 mg/kg). This will provide further insight into need clarifications for paragraphs 3.1.2.5 and 3.1.3.6;
- (c) Include ingredients with data on animal species not considered preferred for testing acute toxicity. This addresses issues raised in paragraph 3.1.2.3;

- (d) Take into consideration pH extremes and other factors, such as buffering capacity for skin and eye hazard classes. (Paragraphs 3.2.3.1.2 and 3.2.3.3.4, and Table 3.2.4 for skin and similar paragraphs in Chapter 3.3 on serious eye damage/irritation);
- (e) For sensitization, carcinogenicity, germ cell mutagenicity, and reproductive hazards, include data closer to the cut-off values;
- (f) Incorporate both the concept of the use of test data for mixtures and test data on similar mixtures in the application of bridging principles.
- (g) Use examples of reproductive toxins that include specific effects. That is, include information on developmental effects and effects on fertility for Categories 1 and 2. Also, include ingredients that have effects on lactation in combination with Categories 1 and 2.
- (h) Incorporate the concept of the building block options for STOT to illustrate the possible differences in classification based upon the “Note 1” option or the “Note 3” option.

Conclusions

25. As demonstrated by this exercise, several issues in need of clarification have been raised and several other issues will need to be explored. As the role of the UN/SCEGHS transitions from that of setting the basic provisions of the GHS to that of maintaining the GHS, the Sub-committee will need to be aware of how differences in interpretation will lead to differences in implementation. We will need to ensure that appropriate guidance is available and/or that the language of the GHS text is clear.

Next steps

26. Based on the results, the group will meet to discuss appropriate means to address the issues raised. Possible options are that additional guidance could be provided in the form of a workbook with examples illustrating key points or even recommendations made to the Sub-committee for changes to the GHS document. Other options could be considered, as well.
27. A second phase of this work will be undertaken to explore additional issues related to the clarification of the classification criteria for mixtures. It is recommended that this work continue over the next year, with a goal of providing a recommendation to the Sub-committee by July 2008.

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