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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

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DEVELOPMENT OF GUIDANCE ON THE APPLICATION OF GHS CRITERIA

Correspondence group for 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 outcome of the work undertaken by the Mixtures Correspondence Group. The work of this Correspondence Group (CG) is a continuation of two pilot projects undertaken by members of the UNSCEGHS. The information provided, herein, discusses the third phase of this work. Further information on the two previous phases can be found in UN/SCEGHS/10/INF.5 and UN/SCEGHS/13/INF.6.

Background

2. To help ensure smooth implementation to the GHS, an exercise to test the classification criteria for mixtures' was developed and distributed to Correspondence Group members in October 2007. The purpose of the exercise was to see if the mixtures' criteria would be applied consistently. The exercise provided data on ingredients for hypothetical mixtures. Correspondence Group members were requested to classify the mixtures based upon that data and the GHS instructions.

3. The results of this exercise indicated that different conclusions were sometimes reached. To discuss these differences, a meeting of the Correspondence Group was held on the sidelines of the proceedings of the fourteenth session of the Sub-Committee of experts on the GHS (December 2007). The purpose of this meeting was to understand and resolve differences.

Process

4. Minutes of the December meeting were distributed for review and approval; and subsequently, a paper was distributed to the Correspondence Group that proposed recommendations to clarify the GHS mixtures' criteria. These recommendations were based on the comments and the participation of Correspondence Group members. Two teleconferences were held to refine the paper. A meeting of the Correspondence Group will also be held on the sidelines of the fifteenth session of the UNSCEGHS.

Proposed recommendations/Conclusions

5. The following recommendations, as presented below, will be provided for consideration by the UNSCEGHS. These recommendations fall into four categories: 1) Develop clarifications to the text of the GHS; 2) Recommend worked examples suggested for inclusion in the UNITAR training documents; 3) Refer the issue to the newly formed Implementation Correspondence Group for consideration; and 4) No action necessary.

Next steps

6. Pending the outcome of discussions at the meeting of the Correspondence Group during the UNSCEGHS lunch break on 10 July 2008, the group plans to submit a formal paper for the sixteenth session of the UNSCEGHS. This paper will recommend editorial clarifications to the text of the GHS and approval of the worked examples as guidance for application of the mixtures' criteria.

Addendum 1

Bridging principles

1. **Background:** At issue was the meaning of the word “and”; that is, whether “and” could be interpreted as “and/or”. The phrase under discussion was, "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…"

   Proposed recommendation: That the SCEGHS approve the editorial clarifications as found in Addendum 1 of this paper. These modifications maintain the meaning of the GHS and indicate that one must have both data on a similar mixture AND sufficient data on the individual ingredients to apply the bridging principles. If there is no test data on a similar mixture, then all one has is information on ingredients. In that case, the Bridging Principles can be skipped all together as the criteria under the heading "estimate hazard(s) on the known ingredient information" are applicable. The Correspondence Group considered that one reason for the confusion regarding application of the bridging principles was the inclusion of the second paragraph in 3.1.3.5.2 (Dilution bridging principle). This paragraph is an application of the ATE calculation and is, therefore, suggested for removal from this chapter. Other changes to the bridging principles are editorial only and provide consistency throughout the health-hazard classification chapters. These changes are noted by “strike-out” marks (deletions) and underlined text (additions).

Acute toxicity

2. **Background:** Results from the mixtures’ criteria exercise, showed that participants did not consistently apply the guidance in Note (a) to Table 3.1.1, which specifies an order of precedence for use of data. Some participants used the conversion values from Table 3.1.2, although LD50 data was provided.

   Proposed recommendation: To request the SCEGHS to approve clarifying modifications of the language of the GHS as highlighted below in Footnote (a) to Table 3.1.1 and paragraph 3.1.3.6.1; to add a clarifying paragraph 3.1.3.3(c) and to edit the heading for Table 3.1.2. A worked example of the application of Table 3.1.2 will also be provided; specifically to demonstrate application of data when existing data do not “fit” the ranges specified in Table 3.1.2. Proposed solutions are listed in order, below:

   Notes to Table 3.1.1:

   (a) The acute toxicity estimate (ATE) for the classification of a substance or ingredient in a mixture is derived using:

   (i) the LD_{50}/LC_{50} where available. Otherwise,

   (ii) the appropriate conversion value from Table 3.1.2 that relates to the results of a range test, or

   (iii) the appropriate conversion value from Table 3.1.2 that relates to a classification category;

3.1.3.6.1 Data available for all ingredients

In order to ensure that classification of the mixture is accurate, and that the calculation need only be performed once for all systems, sectors, and categories, the acute toxicity estimate (ATE) of ingredients should be considered as follows:

(a) Include ingredients with a known acute toxicity, which fall into any of the GHS acute toxicity categories;

(b) Ignore ingredients that are presumed not acutely toxic (e.g. water, sugar);

(c) Ignore ingredients if the oral limit test does not show acute toxicity at 2000 mg/kg bodyweight.

Ingredients that fall within the scope of this paragraph are considered to be ingredients with a known acute toxicity estimate (ATE). See footnote (a) to Table 3.1.1 and paragraph 3.1.3.3 for appropriate application of available data to the equation below and paragraph 3.1.3.6.2.3.

The ATE of the mixture is determined by calculation from the ATE values for all relevant ingredients according to the following formula below for oral, dermal or inhalation toxicity:

$$\frac{100}{\text{ATEmix}} = \sum_{n} \frac{Ci}{\text{ATE}_i}$$

where:

C_i= concentration of ingredient i
n ingredients and i is running from 1 to n
ATE_i = Acute toxicity estimate of ingredient i.

3.1.3.3 In order to make use of all available data for purposes of classifying the hazards of mixtures, certain assumptions have been made and are applied where appropriate in the tiered approach:

(a) The “relevant ingredients” ….Category 1 and Category 2;

(b) Where a ….formulas in 3.1.3.6.1 and 3.1.3.6.2.3.

(c) When only range data (or acute toxicity hazard category information) are available for ingredients in a mixture, they may be converted to point estimates in accordance with Table 3.1.2 when calculating the classification of the new mixture using the formulae in 3.1.3.6.1 and 3.1.3.6.2.3.

Table 3.1.2: Conversion from experimentally obtained acute toxicity range values (or acute toxicity hazard categories) to acute toxicity point estimates for use in the mixtures' classification formulae ~~for the respective routes of exposure~~

(The table is not reprinted here as the changes include only editorial changes to the heading of Table 3.1.2 only.)

Worked example requested:

Ingredient Information:

Ingredient	***Wt%***	***Test Data***
Ingredient 1	*16*	*LD50: 1,600 mg/kg*
Ingredient 2	*4*	*Acute toxicity range estimate: 200 < LD_{50} < 2,000*
Ingredient 3	*80*	*LD50: 3,450 mg/kg*

Answer:
Apply the equation in paragraph 3.1.3.6.1:

$$\frac{100}{ATE_{mixture}} = \sum_{n} \frac{Ci}{ATEi}$$

$$\frac{100}{ATE_{mixture}} = \frac{16}{1{,}600} + \frac{4}{200} + \frac{80}{3{,}450}$$

Therefore: $ATE_{mixture}$ = 1,880 mg/kg, Category 4

See rationale below:

1) *Classification via application of substance criteria is not possible since acute toxicity test data was not provided for the mixture (paragraph 3.1.3.4).*
2) *Classification via the application of bridging principles is not possible since data on a similar mixture was not provided (paragraph 3.1.3.5.1).*
3) *Classification of the mixture based on ingredient data can be considered (paragraph 3.1.3.6).*
4) *Applying the "relevant ingredients" concept from paragraph 3.1.3.3 means that all ingredients will be considered when applying criteria in paragraph 3.1.3.6.1*
5) *Data is available for all ingredients so criteria in paragraph 3.1.3.6.1 apply.*
6) *Ingredients 1, 2 & 3 are all included in the $ATE_{mixture}$ calculation because they have data that fall within a GHS acute toxicity category [Paragraph 3.1.3.6.1 (a)].*
7) *Applying the guidance in Note (a) to Table 3.1.1:*
    a. *The actual LD50 data for Ingredients 1 & 3 are used in the $ATE_{mixture}$ calculation since data are available.*
    b. *The use of Expert Judgment is needed to determine what value to use in the $ATE_{mixture}$ calculation for Ingredient 2. Since the experimentally obtained acute toxicity range estimate of 200 < LD_{50} < 2,000 for Ingredient 2 is existing data developed prior to development of the GHS criteria it does not match up with the ranges provided in Table 3.1.2. The lower end of the range falls within the Category 3 range of 50 – 300 mg/kg and the converted acute toxicity point estimate for an Oral Category 3 ingredient is 100. Given that the converted point estimate is lower than the experimentally*

determined value of > 200 mg/kg it does not make sense to use the converted point estimate. In this case 200 mg/kg should be used in the $ATE_{mixture}$ calculation.

3. **Background:** Participants did not consistently apply the "relevant ingredients" criteria in paragraph 3.1.3.3(a); thus ingredients were not consistently included or excluded from the ATE calculation.

Proposed Recommendation: The following example will be suggested for inclusion in the acute toxicity mixtures chapter of UNITAR's training document:

Worked example requested:

Acute Toxicity - Oral
Ingredient Information:

Ingredient	***Wt%***	***Classification***	***Test Data***
Ingredient 1	*4*	*Oral Category 3*	*LD50: 125 mg/kg*
Ingredient 2	*92*	*-*	*No data available*
Ingredient 3	*3*	*Oral Category 4*	*LD50: 1500 mg/kg*
Ingredient 4	*0.9*	*-*	*No data available*
Ingredient 5	*0.1*	*Oral Category 2*	*LD50: 10 mg/kg*

Answer:

Apply the equation in paragraph 3.1.3.6.2.3:

$$\frac{100-\left(\sum C_{unknown} if\ >10\%\right)}{ATE_{mixture}}=\sum_{n}\frac{C_i}{ATE_i}$$

$$\frac{100-(92)}{ATE_{mixture}}=\frac{4}{125}+\frac{3}{1500}$$

Therefore: $ATE_{mixture}$ = 235 mg/kg, Category 3, and
"92% of the mixture consists of an ingredient of unknown toxicity."

See rationale below:

1) *Classification via application of substance criteria is not possible since acute toxicity test data was not provide for the mixture (paragraph 3.1.3.4).*
2) *Classification via the application of bridging principles is not possible since data on a similar mixture was not provided (paragraph 3.1.3.5.1).*
3) *Classification of the mixture based on ingredient data can be considered (paragraph 3.1.3.6).*
4) *Applying the "relevant ingredients" concept from paragraph 3.1.3.3 means that Ingredient 4 could be excluded from both the $ATE_{mixture}$ calculations. This is true for the calculation in either paragraph 3.1.3.6.1 or 3.1.3.6.2.3. This same reasoning could also apply to Ingredient 5, as it is below the "relevant ingredients" threshold; however, the use of expert judgment is necessary to make this decision for Ingredient 5 as it is classified in Category 2. For this example, it was decided that since the percentage of this ingredient is well below the*

threshold (i.e. 0.1%) and the ingredient is classified in Category 2, it would be excluded from the ATE calculation.

5) *The total concentration of ingredients with unknown acute toxicity (i.e. Ingredient 2) is 92%, therefore, the ATEmixture equation in paragraph 3.1.3.6.2.3 must be used. This calculation corrects for ingredients with unknown acute toxicity above 10% of the mixture.*

6) *Ingredients 1 & 3 are included in the ATEmixture calculation because they have data that fall within a GHS acute toxicity category [Paragraph 3.1.3.6.1 (a)].*

7) *Applying the guidance in Note (a) to Table 3.1.1 results in using the actual LD50 data for Ingredients 1 & 3 in the ATEmixture calculation since data are available.*

4. **Background:** Participants did not consistently apply the criteria found in paragraph 3.1.3.6.1(c), "Ignore ingredients if the oral limit test does not show acute toxicity at 2,000 mg/kg bodyweight." Some participants converted the limit dose of >2,000 mg/kg bodyweight to a point estimate, instead of ignoring that ingredient in the calculation.

Proposed recommendation: The same solution proposed for Issue 1, above, will direct classifiers to appropriately apply data. Additionally, the following example will be suggested for inclusion in the UNITAR training document.

Worked example requested:

Acute toxicity - Oral
Ingredient Information:

Ingredient	***Wt%***	***Classification***	***Test data***
Ingredient 1	*4*	*Oral Category 4*	*LD50: 1,737 mg/kg*
Ingredient 2	*5*	*-*	*LD50: > 5,000 mg/kg*
Ingredient 3	*5*	*-*	*LD50: 5,400 mg/kg*
Ingredient 4	*86*	*-*	*Oral Limit Dose > 2,000 mg/kg (No signs of toxicity)*

Answer:
Apply the equation in paragraph 3.1.3.6.1:

$$\frac{100}{ATE_{mixture}} = \sum_{n} \frac{Ci}{ATEi}$$

$$\frac{100}{ATE_{mixture}} = \frac{4}{1{,}737}$$

Therefore: $ATE_{mixture}$ = 43,425 mg/kg, Not Classified

See rationale below:

1) *Classification via application of substance criteria is not possible since acute toxicity test data was not provide for the mixture (paragraph 3.1.3.4).*
2) *Classification via the application of bridging principles is not possible since data on a similar mixture (paragraph 3.1.3.5.1) was not provided.*
3) *Classification of mixture based ingredient data can be considered (paragraph 3.1.3.6).*
4) *Applying the "relevant ingredients" concept from paragraph 3.1.3.3 means that all ingredients will be considered when applying criteria in paragraph 3.1.3.6.1.*
5) *Data is available for all ingredients so criteria in paragraph 3.1.3.6.1 apply.*
6) *Applying bullet (a) of paragraph 3.1.3.6.1:*
   a. Ingredient 1 is included in the $ATE_{mixture}$ calculation because it falls into a GHS acute toxicity category.
   b. Ingredients 2 and 3 can be ignored in the $ATE_{mixture}$ calculation because they do not fall within a GHS acute toxicity category.
7) *Applying bullet (c) of paragraph 3.1.3.6.1:*
   a. Ingredient 4 can be ignored in the $ATE_{mixture}$ calculation because it has oral limit dose test data that does not show acute toxicity at 2,000 mg/kg.

5. Background: As in Issue 4, above, participants did not consistently apply the criteria in paragraph 3.1.3.6.1(c), "Ignore ingredients if the *oral* limit test does not show acute toxicity at 2,000 mg/kg bodyweight." In one example, participants ignored an ingredient with *dermal* limit dose data even though the criteria only refer to *oral* limit dose test data.

Proposed recommendation: To modify paragraph 3.1.3.6.1(c) to include the two other routes of exposure and consideration of gases, vapors, and dusts. The clarifying, modified language will be proposed as follows:

3.1.3.6.1 Data available for all ingredients

In order to ensure that classification of the mixture is accurate, and that the calculation need only be performed once for all systems, sectors, and categories, the acute toxicity estimate (ATE) of ingredients should be considered as follows:

(a) Include ingredients with a known acute toxicity, which fall into any of the GHS acute toxicity categories;

(b) Ignore ingredients that are presumed not acutely toxic (e.g. water, sugar);

(c) Ignore ingredients if ~~the oral~~ the data available are from a limit dose test (at the upper threshold for Category 4 for the appropriate route of exposure as provided in Table 3.1.1) ~~does~~ and do not show acute toxicity ~~at 2000 mg/kg bodyweight~~.

6. Background: Participants extrapolated between routes of exposure, as provided in the criteria in paragraph 3.1.3.6.2.1, to derive a conversion value despite the lack of sufficient data to apply these criteria.

Proposed recommendation: Application of paragraph 3.1.3.6.2.1 may need to be addressed as the GHS is implemented. It was recognized that this will require a significant level of effort as the application of these criteria would be directed toward highly trained and experienced experts. This may be a future issue for the newly formed Implementation Correspondence Group, but will not be addressed by the Mixtures' Correspondence Group, as it is outside of our current resources and time constraints.

7. **Background:** The criteria in paragraph 3.1.3.2 provides for classification of mixtures for acute toxicity based on each route of exposure, but allows classification to be based on only one route of exposure, provided this route is followed for all ingredients, and all available information is considered. If acute toxicity is determined for more than one route of exposure, it specifies that the most severe category will be used for classification but that "all routes of exposure should be identified for hazard communication." This paragraph is unclear and different interpretations of the criteria may result in inconsistent and incomplete hazard communication.

   ***Proposed recommendation:** One possible path forward that would maintain the option provided by the paragraph while addressing the potential implementation/enforcement problem would be to provide a clarifying change in the language of the paragraph as 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 and there is no relevant evidence to suggest acute toxicity by multiple routes. ~~*If acute toxicity is determined for more than one route of exposure, the more severe hazard category will be used for classification.*~~ *When there is relevant evidence of toxicity by multiple routes of exposure, classification is to be conducted for all appropriate routes of exposure. All available information should be considered. The pictogram and signal word used should reflect the most severe hazard category; and all relevant* ~~*routes of exposure*~~ *hazard statements should be* ~~*identified for hazard communication*~~ *used.*

   *One participant disagreed that this language represented the same meaning as the original. This will be discussed further during the CG meeting on 10 July 08.

8. **Background:** When more than one route of exposure is evaluated according to paragraph 3.1.3.2, it is possible that the classification of a mixture will fall into different GHS categories. This raises the question of the appropriate classification of the mixture. For example, if a mixture is both a Dermal Category 5 and an Inhalation Category 4, how should this mixture be classified? Should the mixture be 1) Acute Toxicity Category 4 or 2) Acute Dermal Toxicity Category 5 and Acute Inhalation Toxicity Category 4?

   Proposed recommendation: This was not generally considered an issue about the application of the mixtures criteria but rather a hazard communication issue which would be better addressed by the GHS Sub-Committee. This issue will be referred to the SCEGHS and possibly, the Implementation Correspondence Group for follow-up.

Skin corrosion/Irritation and serious eye damage/eye irritation

9. **Background:** Participants did not appear to consider the instruction given in paragraphs 3.2.3.3.4 and 3.3.3.3.4, the Skin Corrosion/Irritation and Serious Eye Damage/Eye Irritation Chapters

   Proposed recommendation: The following examples will be suggested for inclusion in the "Skin" and "Eye" chapters of UNITAR's training document:

First worked example requested:

Skin corrosion/irritation
Ingredient Information:

Ingredient	*Wt%*	*Classification*	*Ingredient information*
Ingredient 1	*4*	*Skin Category 1*	*pH = 1.8*
Ingredient 2	*5*	*Skin Category 2*	-
Ingredient 3	*5*	*Skin Category 3*	-
Ingredient 4	*86*	-	*No data available*

Mixture Information: *Mixture pH = 4.0*

Answer:
For this mixture, the classification was assigned as a Category 1 because Ingredient 1 (Category 1) is in the mixture at ≥1%

See rationale below:

1) *Classification via application of substance criteria is not possible since test data (other than a pH) was not provided for the mixture (paragraph 3.2.3.1.1).*
2) *The overall mixture pH of 4.0 does not result in classification in Category 1 since this does not fall within the criteria of pH ≤2 or pH ≥11.5 (paragraph 3.2.3.1.2).*
3) *Classification via the application of bridging principles is not possible since data on a similar mixture was not provided (paragraph 3.2.3.2.1).*
4) *Classification of the mixture based on ingredient data can be considered (paragraph 3.2.3.3).*
5) *Ingredient 1 with a pH = 1.8 is an ingredient for which additivity might not apply as described in paragraph 3.2.3.3.4 and summarized in Table 3.2.4. Expert judgment would be needed to determine whether or not additivity applies. Knowledge of the components is important. Given the limited information in this example, the classifier of this mixture chose to apply non-additivity for a conservative approach. Without information on the mode of action of Ingredient 1, the mixture could be corrosive regardless of the overall pH. Therefore, the criteria described in paragraph 3.2.3.3.4 were applied (i.e. "A mixture containing corrosive or irritant ingredients that cannot be classified based on the additivity approach shown in Table 3.2.3, due to chemical characteristics that make this approach unworkable, should be classified as skin Category 1 if it contains ≥ 1% of a corrosive ingredient and as skin Category 2/3 when it contains ≥ 3% of an irritant ingredient").*

Second worked example requested:

Serious eye damage/Eye irritation
Ingredient Information:

Ingredient	*Wt%*	*Classification*	*Ingredient information*
Ingredient 1	*0.5*	*Eye Category 1*	-
Ingredient 2	*3.5*	*Eye Category 2*	*Surfactant*
Ingredient 3	*15*	-	-
Ingredient 4	*15*	-	-
Ingredient 5	*66*	-	*No data available*

Answer:

Mixture is Category 2 because:

1. *Mixture contains 0.5% of an Eye Category 1 which is not ≥ 1% so the mixture is not Category 1*

2. *Mixture contains 3.5% of an Eye Category 2 which is ≥ 3.0% so the mixture is Category 2*

See rationale below:

1. *Classification via application of substance criteria is not possible since test data was not provided for the mixture (paragraph 3.3.3.1).*
2. *Classification considering the pH of the mixture is not possible as the pH was not provided (paragraph 3.3.3.1).*
3. *Classification via the application of bridging principles is not possible since data on a similar mixture was not provided (paragraph 3.3.3.2.1).*
4. *Classification of the mixture based on ingredient data can be considered (paragraph 3.3.3.3).*
5. *Ingredient 2 (Surfactant) is an ingredient for which additivity might not apply as described in paragraph 3.3.3.3.4 and summarized in Table 3.3.4. Expert judgment would be needed to determine whether or not additivity applies. Knowledge of the components is important. Given the limited information in this example, the classifier of this mixture chose to apply non-additivity for a conservative approach. Therefore, the criteria described in paragraph 3.3.3.3.4 apply (i.e., "A mixture containing corrosive or irritant ingredients that cannot be classified based on the additivity approach shown in Table 3.3.3, due to chemical characteristics that make this approach unworkable, should be classified as Eye Category 1 if it contains ≥ 1% of a corrosive ingredient and as Eye Category 2/3 when it contains ≥ 3% of an irritant ingredient").*

10. **Background:** Participants did not consistently apply the "relevant ingredients" criteria, thus ingredients where not consistently included or excluded from the Eye and Skin calculations.

Solution to be proposed to the SCEGHS: The following example will be suggested for inclusion in the "Skin" and "Eye" chapters of UNITAR's training document:

Worked example requested:

Serious eye damage/Eye irritation
Ingredient Information:

Ingredient	***Wt%***	***Classification***	***Ingredient information***
Ingredient 1	*91*	*-*	*-*
Ingredient 2	*5*	*Eye Category 2A*	*-*
Ingredient 3	*3*	*-*	*-*
Ingredient 4	*0.9*	*Eye Category 1*	*-*
Ingredient 5	*0.1*	*-*	*-*

Answer:
Mixture is Category 2 because:

Equations from Table 3.3.3
Category 1 calculations:
1. ∑%Eye Category 1 = 0.9 which is not ≥ 3%

2. ∑%Skin Category 1 = 0.0 which is not ≥ 3%
3. ∑%Skin Category 1 + ∑%Eye Cat 1 = 0.9 which is not ≥ 3%
Category 2 calculations:
4. ∑%Eye Category 1= 0.9 which is not ≥ 1% but < 3%
5. ∑%Skin Category 1 = 0 which is not ≥ 1% but < 3%
6. ∑%Eye Category 2/2A = 5 which is not ≥ 10%
7. (10x ∑%Eye Category 1) + ∑%Eye Category 2/2A = (10 x 0.9) + 5 = 14% which is ≥ 10%

See rationale below:

1) *Classification via application of substance criteria is not possible since test data was not provided for the mixture (paragraph 3.3.3.1).*
2) *Classification considering pH of the mixture is not possible as the pH was not provided (paragraph 3.3.3.1).*
3) *Classification via the application of bridging principles is not possible since data on a similar mixture was not provided (paragraph 3.3.3.2.1).*
4) *Classification of the mixture based on ingredient data can be considered (paragraph 3.3.3.3).*
5) *Expert judgment is necessary when applying the "relevant ingredients" concept from paragraph 3.3.3.3.1 since Ingredient 4 (Eye Category 1) is below 1%. In this case the relatively high concentration of Ingredient 4 (i.e., 0.9%) and application of the additivity approach which includes a weighting factor for Category 1 ingredients weighs in favor of including Ingredient 4 in the additivity calculations. In fact, for this particular example if ingredient 4 was not considered relevant and was ignored during the calculations the mixture would not be classified because the concentration of Ingredient 2 (Eye Category 2A) is not high enough to cause the additivity equations in Table 3.3.3 to exceed the cut-off value/concentration limits.*
6) *The additivity approach described in Paragraphs 3.3.3.3.2 and 3.3.3.3.3 applies and the cut-off value/concentration limits provided in Table 3.3.3 are used for classification.*

Reproductive toxicity

11. **Background:** Participants did not consistently report the classification of a mixture when it contained two ingredients, both of which were greater than the cut-off/concentration limits. Ingredient 1 was classified as Category 1A. The test data indicated only effects on fertility. Ingredient 2 was classified as Category 2 and had data indicating only developmental effects. In this exercise, the results of classification and the hazard communication elements were reported as Category 1, Category 1A and Category 1A/Category 2.

Proposed recommendation: This issue was not considered to be about the application of the mixtures' criteria, but rather a hazard communication issue which would be better addressed by the GHS Sub-Committee and possibly referred to the Implementation Correspondence Group for follow-up.

12. **Background:** Participants' selection of hazard statements was inconsistent with the "plain language" of the GHS, and in some cases modified the GHS hazard statement text.

Proposed recommendation: This issue was not considered to be about the application of the mixtures' criteria, but rather a hazard communication issue which would be better addressed by the GHS Sub-Committee and possibly referred to the Implementation Correspondence Group for follow-up.

Specific target organ toxicity

13. **Background:** The exercise tested whether there was need for clarification of the method for evaluating transient effects (i.e., narcotic effects and respiratory irritation). Most participants applied an additivity approach to paragraph 3.8.3.4.5 for Category 3 ingredients, even though the criteria do not address additivity.

Proposed recommendation: In addition to providing the example presented below, the GHS language could be edited to indicate that an additivity approach should generally be used for evaluation of transient effects. Suggested clarifying language and the example follow:

3.8.3.4.5
Care should be exercised when extrapolating the toxicity of a mixture that contains Category 3 ingredient(s). A cut-off value/concentration limit of 20% has been suggested; however, it should be recognized that this cut-off value concentration limit may be higher or less depending on the Category 3 ingredient(s) and that some effects such as respiratory tract irritation may not occur below a certain concentration while other effects such as narcotic effects may occur below this 20% value. Expert judgment should be exercised. Respiratory tract irritation and narcotic effects are to be evaluated separately based upon the criteria in paragraph 3.8.2.2. When conducting classifications for these hazards, the contribution of each ingredient should be considered additive, unless there is reason to believe that the effects are not additive.

Worked Example Requested:

Specific Target Organ Toxicity – Single Exposure
Ingredient Information:

Ingredient	***Wt%***	***Classification***
Ingredient 1	*0.5*	*-*
Ingredient 2	*3.5*	*Category 3 – Respiratory Tract Irritation*
Ingredient 3	*15*	*Category 3 - Narcotic effects*
Ingredient 4	*15*	*Category 3 - Narcotic effects*
Ingredient 5	*66*	*-*

Answer:
Mixture is Category 3 – Narcotic effects
∑%Category 3 – Narcotic effects = 15% + 15% = 30% which is > 20%%, therefore classify as Category 3 – Narcotic Effects
∑%Category 3 – Respiratory Irritation = 3.5%, which is < 20%, not classified for Respiratory Irritation

See rationale below:

1) *Classification via application of substance criteria is not possible since test data was not provided for the mixture (paragraph 3.8.3.2).*
2) *Classification via the application of bridging principles is not possible since data on a similar mixture was not provided (paragraph 3.8.3.3.1).*
3) *Application of criteria in paragraph 3.8.3.4.5 is used for classification.*

14. **Background:** The issue regarding the appropriate use of human data was raised, although this issue was not the intention of the exercise. Specifically, in the application of paragraph 3.4.3.2, one participant stated that the data provided on human exposure was not sufficiently defined and, therefore, could not be used for the bridging principles.

Proposed recommendation: This issue was not intended for the exercise, and due to time constraints was not discussed sufficiently to develop a path forward. The Subcommittee might consider referring this to the Implementation Correspondence Group, if it is thought that it could create a barrier to consistent implementation.

Addendum 2

Bridging principles by GHS chapter

3.1.3.5 ***Classification of mixtures where acute toxicity test data are not available for the complete mixture: bridging principles***

3.1.3.5.1 Where the mixture itself has not been tested to determine its acute toxicity, but there are sufficient data on both 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.

3.1.3.5.2 *Dilution*

If a tested mixture is diluted with a diluent that has an equivalent or lower toxicity classification than the least toxic original ingredient, and which is not expected to affect the toxicity of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture. Alternatively, the formula explained in 3.1.3.6.1 could be applied.

~~If a mixture is diluted with water or other totally non-toxic material, the toxicity of the mixture can be calculated from test data on the undiluted mixture. For example, if a mixture with an LD_{50} of 1000 mg/kg bodyweight were diluted with an equal volume of water, the LD_{50} of the diluted mixture would be 2000 mg/kg bodyweight.~~

3.1.3.5.3 *Batching*

The toxicity of ~~one~~ a tested production batch of a ~~complex~~ mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product, ~~and~~ when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the toxicity of the batch has changed. If the latter occurs, new classification is necessary.

3.1.3.5.4 *Concentration of highly toxic mixtures*

If a tested mixture is classified in Category 1, and the concentration of the ingredients of the tested mixture that are in Category 1 is increased, the ~~new~~ resulting untested mixture should be classified in Category 1 without additional testing.

3.1.3.5.5 *Interpolation within one toxicity category*

For three mixtures (A, B, & C) with identical ingredients, where mixtures A and B have been tested and are in the same toxicity category; and where untested mixture C has the same toxicologically active ingredients as mixtures A & B but has ~~with~~ concentrations of toxicologically active ingredients intermediate to the concentrations ~~of those ingredients~~ in mixtures A and B, then mixture C is assumed to be in the same toxicity category as A and B.

3.1.3.5.6 *Substantially similar mixtures*

Given the following:

(a) Two mixtures: (i) A + B;
(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on toxicity for A and C are available and substantially equivalent, i.e. they are in the same hazard category and are not expected to affect the toxicity of B;

If mixture (i) or (ii) is already classified based on test data, then the other mixture ~~(ii)~~ can be assigned the same hazard category.

3.1.3.5.7 *Aerosols*

An aerosol form of a mixture may be classified in the same hazard category as the tested, non-aerosolized form of the mixture for oral and dermal toxicity provided the added propellant does not affect the toxicity of the mixture on spraying. Classification of aerosolized mixtures for inhalation toxicity should be considered separately.

3.2.3.2 ***Classification of mixtures when data are not available for the complete mixture: bridging principles***

3.2.3.2.1 Where the mixture itself has not been tested to determine its skin irritation/corrosion, but there are sufficient data on both 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.

3.2.3.2.2 *Dilution*

If a tested mixture is diluted with a diluent which has an equivalent or lower corrosivity/irritancy classification than the least corrosive/irritant original ingredient and which is not expected to affect the corrosivity/irritancy of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture. Alternatively, the method explained in 3.2.3.3 could be applied.

3.2.3.2.3 *Batching*

The irritation/corrosion potential of ~~one~~ a tested production batch of a ~~complex~~ mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product when ~~and~~ produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the toxicity of the untested batch has changed. If the latter occurs, new classification is necessary.

3.2.3.2.4 *Concentration of mixtures of the highest corrosion/ irritation category*

If a tested mixture classified in the highest sub-category for corrosion is concentrated, ~~a~~the more concentrated untested mixture should be classified in the highest corrosion sub-category without additional testing. If a tested mixture classified in the highest category for skin irritation is concentrated and does not contain corrosive ingredients, ~~a~~ the more concentrated untested mixture should be classified in the highest irritation category without additional testing.

3.2.3.2.5 *Interpolation within one toxicity category*

For three mixtures (A, B, & C) with identical ingredients, where mixtures A and B have been tested and are in the same irritation/corrosion toxicity category; and where untested mixture C has the same toxicologically active ingredients as mixtures A & B but has ~~with~~ concentrations of the toxicologically active ingredients intermediate to the concentrations ~~of those ingredients~~ in mixtures A and B, then mixture C is assumed to be in the same irritation/corrosion category as A and B.

3.2.3.2.6 *Substantially similar mixtures*

Given the following:

(a) Two mixtures: (i) A +B;
(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on irritation/corrosion for A and C are available and substantially equivalent, i.e. they are in the same hazard category and are not expected to affect the toxicity of B.

If mixture (i) or (ii) is already classified based on test data, then the other mixture ~~(ii)~~ can be classified in the same hazard category.

3.2.3.2.7 *Aerosols*

An aerosol form of a mixture may be classified in the same hazard category as the tested non-aerosolized form of mixture provided that the added propellant does not affect the irritation or corrosive properties of the mixture upon spraying.

3.3.3.2 ***Classification of mixtures when data are not available for the complete mixture: bridging principles***

3.3.3.2.1 Where the mixture itself has not been tested to determine its skin corrosivity or potential to cause serious eye damage or irritation, but there are sufficient data on both 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.

3.3.3.2.2 *Dilution*

If a tested mixture is diluted with a diluent which has an equivalent or lower classification for serious eye damage/irritancy classification than the least damaging/irritant original ingredient and which is not expected to affect the corrosivity/irritancy of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture. Alternatively, the method explained in 3.3.3.3 could be applied.

3.3.3.2.3 *Batching*

The irritation/serious eye damage potential of ~~one~~ a tested production batch of a ~~complex~~ mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product ~~and~~ when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the toxicity of the untested batch has changed. If the latter occurs, new classification is necessary.

3.3.3.2.4 *Concentration of mixtures of the highest serious eye damage/ irritation category*

If a tested mixture classified in the highest category for serious eye damage is concentrated, ~~a~~the more concentrated untested mixture should be classified in the highest serious eye damage category without additional testing. If a tested mixture classified in the highest sub-category for skin/eye irritation is concentrated and does not contain serious eye damage ingredients, ~~a~~the more concentrated untested mixture should be classified in the highest irritation category without additional testing.

3.3.3.2.5 *Interpolation within one toxicity category*

For three mixtures (A, B & C) with identical ingredients, where mixtures A and B have been tested and are in the same irritation/ serious eye damage toxicity category; and where untested mixture C has the same toxicologically active ingredients as mixtures A and B but has ~~with~~ concentrations of toxicologically active ingredients intermediate to the concentrations ~~of those ingredients~~ in mixtures A and B, then mixture C is assumed to be in the same irritation/serious eye damage category as A and B.

3.3.3.2.6 *Substantially similar mixtures*

Given the following:

(a) Two mixtures: (i) A +B
(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on irritation/serious eye damage for A and C are available and substantially equivalent, i.e. they are in the same hazard category and are not expected to affect the toxicity of B.

If mixture (i) or (ii) is already classified by testing, then the other mixture ~~(ii)~~ can be assigned in the same hazard category.

3.3.3.2.7 *Aerosols*

An aerosol form of a mixture may be classified in the same hazard category as the tested non-aerosolized form of mixture provided that the added propellant does not affect the irritation or corrosive properties of the mixture upon spraying[1].

[1] *Bridging principles apply for the intrinsic hazard classification of aerosols, however, the need to evaluate the potential for "mechanical" eye damage from the physical force of the spray is recognized.*

3.4.3.2 ***Classification of mixtures when data are not available for the complete mixture: bridging principles***

3.4.3.2.1 Where the mixture itself has not been tested to determine its sensitizing properties, but there are sufficient data on both 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.

3.4.3.2.2 *Dilution*

If a tested mixture is diluted with a diluent which is not a sensitizer and which is not expected to affect the sensitization of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture.

3.4.3.2.3 *Batching*

The sensitizing properties of ~~one~~ a tested production batch of a ~~complex~~ mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product ~~and~~ when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the sensitization potential of the untested batch has changed. If the latter occurs, new classification is necessary.

3.4.3.2.4 *Substantially similar mixtures*

Given the following:

(a) Two mixtures: (i) A + B;
(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Ingredient B is a sensitizer and ingredients A and C are not sensitizers;

(e) A and C are not expected to affect the sensitizing properties of B.

If mixture (i) or (ii) is already classified by testing, then the other mixture ~~(ii)~~ can be assigned the same hazard category.

3.4.3.2.5 *Aerosols*

An aerosol form of the mixture may be classified in the same hazard category as the tested non-aerosolized form of the mixture provided that the added propellant does not affect the sensitizing properties of the mixture upon spraying.

3.5.3.2 ***Classification of mixtures when data are not available for the complete mixture: bridging principles***

3.5.3.2.1 Where the mixture itself has not been tested to determine its germ cell mutagenicity hazard, but there are sufficient data on both 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.

3.5.3.2.2 *Dilution*

If a tested mixture is diluted with a diluent which is not expected to affect the germ cell mutagenicity of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture.

3.5.3.2.3 *Batching*

The germ cell mutagenic potential of a tested ~~one~~ production batch of a ~~complex~~ mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product when produced by ~~and~~ or under the control of the same manufacturer unless there is reason to believe there is significant variation in composition such that the germ cell mutagenic potential of the untested batch has changed. If the latter occurs, a new classification is necessary.

3.5.3.2.4 *Substantially similar mixtures*

Given the following:

(a) Two mixtures: (i) A + B;
(ii) C + B;

(b) The concentration of mutagen ingredient B is the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on toxicity for A and C are available and substantially equivalent, i.e. they are in the same hazard category and are not expected to affect the germ cell mutagenicity of B.

If mixture (i) or (ii) is already classified by testing, then the other mixture ~~(ii)~~ can be classified in the ~~same~~ same hazard category.

3.6.3.2 ***Classification of mixtures when data are not available for the complete mixture: bridging principles***

3.6.3.2.1 Where the mixture itself has not been tested to determine its carcinogenic hazard, but there are sufficient data on both 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.

3.6.3.2.2 *Dilution*

If a tested mixture is diluted with a diluent that is not expected to affect the carcinogenicity of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture.

3.6.3.2.3 *Batching*

The carcinogenic potential of ~~one~~ a tested production batch of a ~~complex~~ mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product when produced by or ~~and~~ under the control of the same manufacturer unless there is reason to believe there is significant variation in composition such that the carcinogenic potential of the untested batch has changed. If the latter occurs, a new classification is necessary.

3.6.3.2.4 *Substantially similar mixtures*

Given the following:

(a) Two mixtures: (i) A + B;
(ii) C + B;

(b) The concentration of carcinogen ingredient B is the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on toxicity for A and C are available and substantially equivalent, i.e. they are in the same hazard category and are not expected to affect the carcinogenicity of B.

If mixture (i) or (ii) is already classified by testing, then the other mixture ~~(ii)~~ can be assigned the same hazard category.

3.7.3.2 ***Classification of mixtures when data are not available for the complete mixture: bridging principles***

3.7.3.2.1 Where the mixture itself has not been tested to determine its reproductive toxicity, but there are sufficient data on both 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 rules. 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.

3.7.3.2.2 *Dilution*

If a tested mixture is diluted with a diluent which is not expected to affect the reproductive toxicity of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture.

3.7.3.2.3 *Batching*

The reproductive toxicity potential of ~~one~~ a tested production batch of a ~~complex~~ mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product when produced by or ~~and~~ under the control of the same manufacturer unless there is reason to believe there is significant variation in composition such that the reproductive toxicity potential of the untested batch has changed. If the latter occurs, a new classification is necessary.

3.7.3.2.4 *Substantially similar mixtures*

Given the following:

(a) Two mixtures: (i) A + B;
(ii) C + B;

(b) The concentration of Ingredient B, toxic to reproduction, is the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on toxicity for A and C are available and substantially equivalent, i.e. they are in the same hazard category and are not expected to affect the reproductive toxicity of B.

If mixture (i) or (ii) is already classified by testing, then the other mixture ~~(ii)~~ can be assigned the same hazard category.

3.8.3.3 ***Classification of mixtures when data are not available for the complete mixture: bridging principles***

3.8.3.3.1 Where the mixture itself has not been tested to determine its specific target organ toxicity, but there are sufficient data on both the individual ingredients and similar tested mixtures to adequately characterize the hazards of the mixture, these data can be used in accordance with the following 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 of additional testing in animals.

3.8.3.3.2 *Dilution*

If a tested mixture is diluted with a diluent which has the same or a lower toxicity classification as the least toxic original ingredient and which is not expected to affect the toxicity of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture.

3.8.3.3.3 *Batching*

The toxicity of ~~one~~ a tested production batch of a ~~complex~~ mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product when ~~and~~ produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the toxicity of the untested batch has changed. If the latter occurs, a new classification is necessary.

3.8.3.3.4 *Concentration of highly toxic mixtures*

If in a tested mixture of Category 1, the concentration of a toxic ingredient is increased, the resulting concentrated mixture should be classified in Category 1 without additional testing.

3.8.3.3.5 *Interpolation within one toxicity category*

For three mixtures (A, B, & C) with identical ingredients, ~~where~~ where mixtures A and B have been tested and are in the same toxicity category; and where untested mixture C has the same toxicologically active ingredients as mixtures A & B but has ~~with~~ concentrations of toxicologically active ingredients intermediate to the concentrations in ~~of those ingredients in~~ mixtures A and B, then mixture C is assumed to be in the same toxicity category as A and B.

3.8.3.3.6 Substantially similar mixtures

Given the following:

(a) Two mixtures: (i) A + B;
(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on toxicity for A and C are available and substantially equivalent, i.e. they are in the same hazard category and are not expected to affect the toxicity of B.

If mixture (i) or (ii) is already classified by testing, then the other mixture ~~(ii)~~ can be assigned the same hazard category.

3.8.3.3.7 *Aerosols*

An aerosol form of a mixture may be classified in the same hazard category as the tested, non-aerosolized form of the mixture for oral and dermal toxicity provided the added propellant does not affect the toxicity of the mixture on spraying. Classification of aerosolized mixtures for inhalation toxicity should be considered separately.

3.9.3.3 ***Classification of mixtures when data are not available for the complete mixture: bridging principles***

3.9.3.3.1 Where the mixture itself has not been tested to determine its specific target organ toxicity, but there are sufficient data on both the individual ingredients and similar tested mixtures to adequately characterize the hazards of the mixture, these data can be used in accordance with the following 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 of additional testing in animals.

3.9.3.3.2 *Dilution*

If a tested mixture is diluted with a diluent which has the same or a lower toxicity classification as the least toxic original ingredient and which is not expected to affect the toxicity of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture.

3.9.3.3.3 *Batching*

The toxicity of ~~one~~ a tested production batch of a ~~complex~~ mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product ~~and~~ when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the toxicity of the untested batch has changed. If the latter occurs, new classification is necessary.

3.9.3.3.4 *Concentration of highly toxic mixtures*

If in a tested mixture of Category 1, the concentration of a toxic ingredient is increased, the resulting concentrated mixture should be classified in Category 1 without additional testing.

3.9.3.3.5 *Interpolation within one toxicity category*

For three mixtures (A, B, & C) with identical ingredients, where mixtures A and B have been tested and are in the same toxicity category; and where untested mixture C has the same toxicologically active ingredients as mixtures A and B but has ~~with~~ concentrations of toxicologically active ingredients intermediate to the concentrations ~~of those ingredients~~ in mixtures A and B, then mixture C is assumed to be in the same toxicity category as A and B.

3.9.3.3.6 *Substantially similar mixtures*

Given the following:

(a) Two mixtures: (i) A + B;

(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on toxicity for A and C are available and substantially equivalent, i.e. they are in the same hazard category and are not expected to affect the toxicity of B.

If mixture (i) or (ii) is already classified by testing, then the other mixture ~~(ii)~~ can be assigned the same hazard category.

3.9.3.3.7 *Aerosols*

An aerosol form of a mixture may be classified in the same hazard category as the tested, non-aerosolized form of the mixture for oral and dermal toxicity provided the added propellant does not affect the toxicity of the mixture on spraying. Classification of aerosolized mixtures for inhalation toxicity should be considered separately.

3.10.3.2 ***Classification of mixtures when data are not available for the complete mixture: bridging principles***

3.10.3.2.1 Where the mixture itself has not been tested to determine its aspiration toxicity, but there are sufficient data on both the individual ingredients and similar tested mixtures to adequately characterize the hazard of the mixture, these data will be used in accordance with the following 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 of additional testing in animals.

3.10.3.2.2 *Dilution*

If a tested mixture is diluted with a diluent that does not pose an aspiration toxicity hazard, and which is not expected to affect the aspiration toxicity of other ingredients or the mixture, then the new diluted mixture may be classified as equivalent to the original tested mixture. However, the concentration of aspiration toxicant(s) should not drop below 10%.

3.10.3.2.3 Batching

The aspiration toxicity of a tested ~~one~~ production batch of a ~~complex~~ mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product~~,~~ when ~~and~~ produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the aspiration toxicity, reflected by viscosity or concentration, of the untested batch has changed. If the latter occurs, new classification is necessary.

3.10.3.2.4 *Concentration of Category 1 mixtures*

If a tested mixture is classified in Category 1, and the concentration of the ingredients of the tested mixture that are in Category 1 is increased, the resulting untested ~~new~~ mixture should be classified in Category 1 without additional testing.

3.10.3.2.5 *Interpolation within one toxicity category*

For three mixtures (A, B, & C) with identical ingredients, where mixtures A and B have been tested and are in the same toxicity category; and where untested mixture C has the same toxicologically active ingredients as mixtures A and B but has ~~with~~ concentrations of toxicologically active ingredients intermediate to the concentrations ~~of those ingredients~~ in mixtures A and B, then mixture C is assumed to be in the same toxicity category as A and B.

3.10.3.2.6 *Substantially similar mixtures*

Given the following:

(a) Two mixtures: (i) A + B;
(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Aspiration toxicity for A and C is substantially equivalent, i.e. they are in the same hazard category and are not expected to affect the aspiration toxicity of B.

If mixture (i) or (ii) is already classified based on the criteria in table 3.10.1, then the other mixture ~~(ii)~~ can be assigned the same hazard category.

4.1.3.4 *Classification of mixtures when data are not available for the complete mixture: bridging principles*

4.1.3.4.1 Where the mixture itself has not been tested to determine its aquatic environmental hazard, but there are sufficient data on both the individual ingredients and similar tested mixtures to adequately characterize the hazards of the mixture, this 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.

4.1.3.4.2 *Dilution*

~~If~~ **Where** a **new** mixture is formed by diluting a~~nother~~ ~~classified~~ **tested** mixture or a substance with a diluent which has an equivalent or lower aquatic hazard classification than the least toxic original ingredient and which is not expected to affect the aquatic hazards of other ingredients, then the **resulting** mixture may be classified as equivalent to the original **tested** mixture or substance.
~~If a mixture is formed by diluting another classified mixture or a substance with water or other totally non-toxic material, the toxicity of the mixture can be calculated from the original mixture or substance.~~ **Alternatively, the method explained in 4.1.3.5 could be applied.**

4.1.3.4.3 *Batching*

The aquatic hazard classification of ~~one~~ **a tested** production batch of a mixture can be assumed to be substantially equivalent to that of another **untested** production batch of the same commercial product ~~and~~ when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the aquatic hazard classification of the **untested** batch has changed. If the latter occurs, a new classification is necessary.

4.1.3.4.4 *Concentration of mixtures which are classified with the most severe classification categories (Chronic 1 and Acute 1)*

If a **tested** mixture is classified as Chronic 1 and/or Acute 1, and **the** ingredients of the mixture which are classified as Chronic 1 and/or Acute 1 are further concentrated, the more concentrated **untested** mixture should be classified with the same classification category as the original **tested** mixture without additional testing.

4.1.3.4.5 *Interpolation within one toxicity category*

~~If mixtures A and B are in the same classification category and mixture C is made in which the toxicologically active ingredients have concentrations intermediate to those in mixtures A and B, then mixture C is assumed to be in the same category as A and B. Note that the identity of the ingredients is the same in all three mixtures.~~

For three mixtures (A, B, & C) with identical ingredients, where mixtures A and B have been tested and are in the same toxicity category; and where untested mixture C has the same toxicologically active ingredients as mixtures A & B but has concentrations of the toxicologically active ingredients intermediate to the concentrations in mixtures A and B, then mixture C is assumed to be in the same toxicity category as A and B.

4.1.3.4.6 *Substantially similar mixtures*

Given the following:

(a) Two mixtures: (i) A + B;
(ii) C + B;

(b) The concentration of ingredient B is **essentially** the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) ~~Classification~~ **Data on aquatic toxicity** for A and C are available and ~~are the same~~ **substantially equivalent**, i.e. they are in the same hazard category and are not expected to affect the aquatic toxicity of B.

~~Then there is no need to test mixture (ii) if mixture (i) is already characterized by testing and both mixtures would be classified in the same category.~~
If mixture (i) or (ii) is already classified based on test data, then the other mixture can be assigned the same hazard category.
