

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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Item 2 (f) of the provisional agenda

Work on the Globally Harmonized System of Classification and Labelling of Chemicals:

**Practical classification issues (proposed amendments
to the Globally Harmonized System)**

Proposals to address issues from the program of work for the practical classification issues correspondence group

**Transmitted by the expert from the United States of America on behalf
of the practical classification issues informal correspondence group**

Purpose

1. This informal document serves as a companion document to set out the changes proposed in document ST/SG/AC.10/C.4/2022/21. The proposed updates are indicated using ~~strikeout~~ and underline font.
2. Amendments to paragraphs 3.2.2.8.1, 3.3.2.10.1 and 3.3.5.3.4.2 in ST/SG/AC.10/C.4/2022/21 refer to the texts consolidated in ST/SG/AC.10/C.4/2022/13, as provisionally adopted by the Sub-Committee at its fortieth session (see ST/SG/AC.10/C.4/80).
3. The Sub-Committee is invited to note that in paragraph 15 (b) in document ST/SG/AC.10/C.4/2022/21, “3.1.3.5.6” should read “3.1.3.5.7” (three times). This correction has been taken into account in this document.

Annex

Proposed amendments to address Item 1

For consistency, the group reviewed the different terms Weight of Evidence (WoE) approach/determination/evaluation/analysis throughout the GHS, and where appropriate, revised the text to WoE “assessment”. As part of the review, it was agreed that in some cases it was more appropriate to retain the term WoE “approach” and as such, these cases are not included in the proposals below.

Chapter 1.3

1.3.2.4.8 Amend as shown:

“1.3.2.4.8 Expert judgement

The approach to classifying mixtures includes the application of expert judgement in a number of areas in order to ensure existing information can be used for as many mixtures as possible to provide protection for human health and the environment. Expert judgement may also be required in interpreting data for hazard classification of substances, especially where weight of evidence ~~determinations~~ assessments are needed.”

1.3.2.4.9.2 Amend as shown:

“1.3.2.4.9.2 The quality and consistency of the data are important. Evaluation of substances or mixtures related to the material being classified should be included, as should site of action and mechanism or mode of action study results. Both positive and negative results are assembled together in a single weight of evidence ~~determination~~ assessment.”

1.3.2.4.9.5 Amend as shown:

“1.3.2.4.9.5 Both positive and negative results are assembled together in the weight of evidence ~~determination~~ assessment. However, a single positive study performed according to good scientific principles and with statistically and biologically significant positive results may justify classification.”

Chapter 3.1

3.1.2.3 Amend as shown:

“3.1.2.3 The preferred test species for evaluation of acute toxicity by the oral and inhalation routes is the rat, while the rat or rabbit are preferred for evaluation of acute dermal toxicity. Test data already generated for the classification of chemicals under existing systems should be accepted when reclassifying these chemicals under the harmonized system. When experimental data for acute toxicity are available in several animal species, scientific judgement should be used in selecting the most appropriate LD₅₀ value from among valid, well-performed tests. In cases where data from human experience (i.e. occupational data, data from accident databases, epidemiology studies, clinical reports) are also available, they should be considered in a weight of evidence ~~approach~~ assessment consistent with the principles described in 1.3.2.4.9.”

Chapter 3.2

3.2.5.3.5.2.6 Amend as shown:

“3.2.5.3.5.2.6 In skin absorption studies (e.g. OECD Test Guideline 427), corrosive exposure conditions are generally avoided as this affects the absorption. Therefore, information on skin effects from these studies does not allow classification directly but may be considered within a weight of evidence ~~approach~~ assessment. However, information on the dermal absorption may be taken into account in a weight-of-evidence assessment as a

high dermal absorption in combination with additional evidence for high cytotoxicity may indicate irritation or corrosivity.”

Chapter 3.4

3.4.2.1.1.3 Amend as shown:

“3.4.2.1.1.3 Effects seen in either humans or animals will normally justify classification in a weight of evidence ~~approach~~ assessment for respiratory sensitizers. Substances may be allocated to one of the two sub-categories 1A or 1B using a weight of evidence ~~approach~~ assessment in accordance with the criteria given in Table 3.4.1 and on the basis of reliable and good quality evidence from human cases or epidemiological studies and/or observations from appropriate studies in experimental animals.”

3.4.3.1 Amend as shown:

“3.4.3.1 Classification of mixtures when data are available for the complete mixture

When reliable and good quality evidence from human experience or appropriate studies in experimental animals, as described in the criteria for substances, is available for the mixture, then the mixture can be classified by weight of evidence ~~evaluation~~ assessment of these data. Care should be exercised in evaluating data on mixtures that the dose used does not render the results inconclusive. (For special labelling required by some competent authorities, see the note to Table 3.4.5 of this chapter and 3.4.4.2.)”

Chapter 3.5

3.5.5.1.1 Decision logic 3.5.1, second and third textbox down, amend as shown:

“Application of the criteria needs expert judgment in a weight of evidence ~~approach~~ assessment.”

Chapter 3.6

3.6.5.3.2 Amend as shown:

“3.6.5.3.2 Guidance on how to consider important factors in classification of carcinogenicity*
 The guidance provides an approach to analysis rather than hard and fast rules. This section provides some considerations. The weight of evidence ~~analysis~~ assessment called for in GHS is an integrative approach which considers important factors in determining carcinogenic potential along with the strength of evidence analysis. The IPCS “Conceptual Framework for Evaluating a Mode of Action for Chemical carcinogenesis” (2001), the International Life Sciences Institute (ILSI) “Framework for Human Relevance Analysis of Information on Carcinogenic Modes of Action” (Meek et al., 2003; Cohen et al., 2003, 2004) and the IARC (Preamble section 12(b)) provide a basis for systematic assessments which may be performed in a consistent fashion internationally; the IPCS also convened a panel in 2004 to further develop and clarify the human relevance framework. However, the internationally available documents are not intended to dictate answers, nor provide lists of criteria to be checked off.

3.6.5.3.2.1 Amend as shown:

“3.6.5.3.2.1 Mode of action

The various international documents on carcinogen assessment all note that mode of action in and of itself, or consideration of comparative metabolism, should be evaluated on a case-by-case basis and are part of an analytic evaluative approach. One must look closely at any mode of action in animal experiments taking into consideration comparative toxicokinetics/toxicodynamics between the animal test species and humans to determine the relevance of the results to humans. This may lead to the possibility of

discounting very specific effects of certain types of chemicals. Life stage-dependent effects on cellular differentiation may also lead to qualitative differences between animals and humans. Only if a mode of action of tumour development is conclusively determined not to be operative in humans may the carcinogenic evidence for that tumour be discounted. However, a weight of evidence ~~evaluation~~ assessment for a substance calls for any other tumorigenic activity to be evaluated as well.”

3.6.5.1 Decision logic 3.6.1 for substances (second and third textbox down), amend as shown:

“Application of the criteria needs expert judgment in a strength and weight of evidence ~~approach~~ assessment.”

Chapter 3.7

3.7.2.2 Amend as shown:

“3.7.2.2 Basis of classification

3.7.2.2.1 Classification is made on the basis of the appropriate criteria, outlined above, and a total weight of evidence assessment ~~an assessment of the total weight of evidence~~. Classification as a reproductive toxicant is intended to be used for chemicals which have an intrinsic, specific property to produce an adverse effect on reproduction and chemicals should not be so classified if such an effect is produced solely as a non-specific secondary consequence of other toxic effects.”

3.7.2.3 Amend as shown:

“3.7.2.3 Weight of evidence

3.7.2.3.1 Classification as a reproductive toxicant is made on the basis of ~~an assessment of the total weight of evidence~~ a total weight of evidence assessment. This means that all available information that bears on the determination of reproductive toxicity is considered together. Included is information such as epidemiological studies and case reports in humans and specific reproduction studies along with sub-chronic, chronic and special study results in animals that provide relevant information regarding toxicity to reproductive and related endocrine organs. Evaluation of substances chemically related to the material under study may also be included, particularly when information on the material is scarce. The weight given to the available evidence will be influenced by factors such as the quality of the studies, consistency of results, nature and severity of effects, level of statistical significance for intergroup differences, number of endpoints affected, relevance of route of administration to humans and freedom from bias. Both positive and negative results are assembled together into a weight of evidence ~~determination~~ assessment. However, a single, positive study performed according to good scientific principles and with statistically or biologically significant positive results may justify classification (see also 3.7.2.2.3).”

3.7.2.4 Amend as shown:

“3.7.2.4 Maternal toxicity

3.7.2.4.1 Development of the offspring throughout gestation and during the early postnatal stages can be influenced by toxic effects in the mother either through non-specific mechanisms related to stress and the disruption of maternal homeostasis, or by specific maternally-mediated mechanisms. So, in the interpretation of the developmental outcome to decide classification for developmental effects it is important to consider the possible influence of maternal toxicity. This is a complex issue because of uncertainties surrounding the relationship between maternal toxicity and developmental outcome. Expert judgement and a weight of evidence ~~approach~~ assessment, using all available studies, should be used to determine the degree of influence that should be attributed to maternal toxicity when interpreting the criteria for classification for developmental effects. The adverse effects in the embryo/foetus should be first considered, and then maternal toxicity, along with any other factors which are likely to have influenced these effects, as weight of evidence, to help reach a conclusion about classification.”

3.7.5.1.1 Decision logic 3.7.1 for substances (second and third textboxes down), amend the sentence below as shown:

“Application of the criteria needs expert judgment in a weight of evidence ~~approach~~ assessment.”

Chapter 3.8

Notes to Table 3.8.1, amend as shown:

^a The guidance values and ranges mentioned in Table 3.8.1. above are intended only for guidance purposes, i.e. to be used as part of the weight of evidence ~~approach~~ assessment, and to assist with decision about classification. They are not intended as strict demarcation values.

^b Guidance values are not provided since this classification is primarily based on human data. Animal data may be included in the weight of evidence ~~evaluation~~ assessment.”

3.8.2.1.10 Amend as shown:

“3.8.2.1.10 Other considerations

3.8.2.1.10.1 When a substance is characterized only by use of animal data (typical of new substances, but also true for many existing substances), the classification process would include reference to dose/concentration guidance values as one of the elements that contribute to the weight of evidence ~~approach~~ assessment.”

3.8.2.2.1 (d) Amend as shown:

“(d) There are currently no validated animal tests that deal specifically with RTI, however, useful information may be obtained from the single and repeated inhalation toxicity tests. For example, animal studies may provide useful information in terms of clinical signs of toxicity (dyspnoea, rhinitis etc) and histopathology (e.g. hyperemia, edema, minimal inflammation, thickened mucous layer) which are reversible and may be reflective of the characteristic clinical symptoms described above. Such animal studies can be used as part of weight of evidence ~~evaluation~~ assessment.”

3.8.3.2 Amend as shown:

“3.8.3.2 Classification of mixtures when data are available for the complete mixture

When reliable and good quality evidence from human experience or appropriate studies in experimental animals, as described in the criteria for substances, is available for the mixture, then the mixture can be classified by weight of evidence ~~evaluation~~ assessment of this data. Care should be exercised in evaluating data on mixtures, that the dose, duration, observation or analysis, do not render the results inconclusive.”

3.8.5.1 Decision logic 3.8.1 (fourth and fifth textbox down), amend the sentence below as shown:

“See 3.8.2 for criteria and guidance values. Application of the criteria needs expert judgment in a weight of evidence ~~approach~~ assessment.”

Decision logic 3.8.1 (sixth textbox down), amend the sentence below as shown:

“See 3.8.2 and 3.8.3 for criteria. Application of the criteria needs expert judgment in a weight of evidence ~~approach~~ assessment.”

Chapter 3.9

3.9.2.9.8 Amend as shown:

“3.9.2.9.8 The guidance values and ranges mentioned in 3.9.2.9.6 and 3.9.2.9.7 are intended only for guidance purposes, i.e. to be used as part of the weight of evidence ~~approach~~ assessment, and to assist with decisions about classification. They are not intended as strict demarcation values.”

3.9.2.10 Amend as shown:

“3.9.2.10 Other considerations

3.9.2.10.1 When a substance is characterized only by use of animal data (typical of new substances, but also true for many existing substances), the classification process would include reference to dose/concentration guidance values as one of the elements that contribute to the weight of evidence ~~approach~~ assessment.”

3.9.3.2 Amend as shown:

“3.9.3.2 Classification of mixtures when data are available for the complete mixture

When reliable and good quality evidence from human experience or appropriate studies in experimental animals, as described in the criteria for substances, is available for the mixture, then the mixture can be classified by weight of evidence ~~evaluation~~ assessment of this data. Care should be exercised in evaluating data on mixtures, that the dose, duration, observation or analysis, do not render the results inconclusive.”

3.9.5.1 Decision logic 3.9.1 fourth and fifth textbox down, amend the sentence below as shown:

“See 3.9.2 for criteria and guidance values¹. Application of the criteria needs expert judgment in a weight of evidence ~~approach~~ assessment.”.

Chapter 4.1

4.1.2.5 Amend as shown:

“4.1.2.5 The system for classification recognizes that the core intrinsic hazard to aquatic organisms is represented by both the acute and chronic toxicity of a substance, the relative importance of which is determined by the specific regulatory system in operation. Distinction can be made between the short-term (acute) hazard and the long-term (chronic) hazard and therefore separate hazard categories are defined for both properties representing a gradation in the level of hazard identified. The lowest of the available toxicity values between and within the different trophic levels (fish, crustacean, algae) will normally be used to define the appropriate hazard category(ies). There may be circumstances, however, when a weight of evidence ~~approach~~ assessment may be used. Acute toxicity data are the most readily available and the tests used are the most standardized.”

Annex 9

A9.4.3.5.1 Amend as shown:

“A9.4.3.5.1 The situation where more degradation data are available for the same substance introduces the possibility of conflicting results. In general, conflicting results for a substance which has been tested several times with an appropriate biodegradability test could be interpreted by a “weight of evidence ~~approach~~ assessment”². This implies that if both positive (i.e. higher degradation than the pass level) and negative results have been obtained for a substance in ready biodegradability tests, then the data of the highest quality and the best documentation should be used for determining the ready biodegradability of the substance. However, positive results in ready biodegradability tests could be considered valid, irrespective of negative results, when the scientific quality is good and the test conditions are well documented, i.e. guideline criteria are fulfilled, including the use of non-pre-exposed (non-adapted) inoculum. None of the various screening tests are suitable for the testing of all types of substances, and results obtained by the use of a test procedure which is not suitable for the specific substance should be evaluated carefully before a decision on the use is taken.”

A9.4.3.6 Amend as shown:

“A9.4.3.6 Variation in simulation test data

A number of simulation test data may be available for certain high priority chemicals. Often such data provide a range of half-lives in environmental media such as soil, sediment and/or surface water. The observed differences in half-lives from simulation tests performed on the same substance may reflect differences in test conditions, all of which may

be environmentally relevant. A suitable half-life in the higher end of the observed range of half-lives from such investigations should be selected for classification by employing a weight of evidence ~~approach~~ assessment and taking the realism and relevance of the employed tests into account in relation to environmental conditions. In general, simulation test data of surface water are preferred relative to aquatic sediment or soil simulation test data in relation to the evaluation of rapid degradability in the aquatic environment.”

A9.5.4.1 Amend as shown:

“A9.5.4.1 Conflicting BCF data

In situations where multiple BCF data are available for the same substance, the possibility of conflicting results might arise. In general, conflicting results for a substance, which has been tested several times with an appropriate bioconcentration test, should be interpreted by a “weight of evidence ~~approach~~ assessment”. This implies that if experimental determined BCF data, both \geq and $<$ 500, have been obtained for a substance the data of the highest quality and with the best documentation should be used for determining the bioconcentration potential of the substance. If differences still remain, if e.g. high-quality BCF values for different fish species are available, generally the highest valid value should be used as the basis for classification.”

Chapter 3.4

The following proposed amendments related to Issue 1 are only needed if the Non-animal Test Methods Working Group’s proposal to amend the hazard class Skin Sensitization in Chapter 3.4 are not adopted.

3.4.2.2.1.3 Amend as shown:

“3.4.2.2.1.3 Effects seen in either humans or animals will normally justify classification in a weight of evidence ~~approach~~ assessment for skin sensitizers as described in 3.4.2.2.2. Substances may be allocated to one of the two sub-categories 1A or 1B using a weight of evidence ~~approach~~ assessment in accordance with the criteria given in Table 3.4.2 and on the basis of reliable and good quality evidence from human cases or epidemiological studies and/or observations from appropriate studies in experimental animals according to the guidance values provided in 3.4.2.2.2.1 and 3.4.2.2.3.2 for sub-category 1A and in 3.4.2.2.2.2 and 3.4.2.2.3.3 for sub-category 1B.”

3.4.2.2.4.1 Amend as shown:

“3.4.2.2.4.1 For classification of a substance, evidence should include any or all of the following ~~using in~~ a weight of evidence ~~approach~~ assessment.”

Proposed amendments to address Item 2

Clarify in paragraphs 3.2.2.8.1, 3.3.2.10.1 and 3.3.5.3.4.2 (as provisionally adopted by the Sub-Committee at its fortieth session (see ST/SG/AC.10/C.4/80) and consolidated in ST/SG/AC.10/C.4/2022/13) the meaning of the term “elements”.

3.2.2.8.1 A tiered approach to the evaluation of ~~initial~~ information should be considered, where applicable (Figure 3.2.1), recognizing that not all ~~elements~~ tiers as well as information within a tier may be relevant. However, all available and relevant information of sufficient quality needs to be examined for consistency with respect to the resulting classification.

3.3.2.10.1 A tiered approach to the evaluation of ~~initial~~ information should be considered, where applicable (Figure 3.3.1), recognizing that not all ~~elements~~ tiers as well as information within a tier may be relevant. However, all available and relevant information of sufficient quality needs to be examined for consistency with respect to the resulting classification.

3.3.5.3.4.2 A stepwise approach to the evaluation of information derived from Tier 2 of Figure 3.3.1, i.e. defined approaches and/or *in vitro/ex vivo* test methods, should be considered where applicable (Figure 3.3.3), recognizing that not all ~~elements~~ tiers as well as information within a tier may

be relevant. However, all available and relevant information of sufficient quality needs to be examined for consistency with respect to the resulting classification. The outcome of a defined approach containing conclusive animal and/or human data may also eventually be considered during the overall weight of evidence in Tier 7 (see Figure 3.3.1). Where information from several steps is inconsistent and/or conflicting with respect to the resulting classification, information of sufficient quality from a higher step is generally given a higher weight than information from a lower step. However, when information from a lower step would result in a stricter classification than information from a higher step and there is concern for misclassification, then classification is determined by a within-tier weight of evidence assessment. For example, classifiers concerned with a negative result for serious eye damage in a defined approach when there is a positive result for serious eye damage in an *in vitro/ex vivo* method would utilise a within-tier weight of evidence assessment.

Proposed amendments to address Item 4

Clarify in paragraphs 3.2.3.3.1 and 3.3.3.3.1 that the use of the term “tiered approach” is referring to the mixture tiered approach and not the substance tiered approach.

Chapter 3.2

3.2.3.3.1 Amend as shown:

“3.2.3.3.1 In order to make use of all available data for purposes of classifying the skin corrosion/irritation hazards of mixtures, the following assumption has been made and is applied where appropriate in the tiered approach to mixtures (see 1.3.2.3):

The “relevant ingredients” of a mixture are those which are present in concentrations $\geq 1\%$ (w/w for solids, liquids, dusts, mists and vapours and v/v for gases), unless there is a presumption (e.g. in the case of corrosive ingredients) that an ingredient present at a concentration $< 1\%$ can still be relevant for classifying the mixture for skin corrosion/irritation.”

Chapter 3.3

3.3.3.3.1 Amend as shown:

“3.3.3.3.1 In order to make use of all available data for purposes of classifying the serious eye damage/eye irritation properties of the mixtures, the following assumption has been made and is applied where appropriate in the tiered approach to mixtures (see 1.3.2.3):

The “relevant ingredients” of a mixture are those which are present in concentrations $\geq 1\%$ (w/w for solids, liquids, dusts, mists and vapours and v/v for gases), unless there is a presumption (e.g. in the case of corrosive ingredients) that an ingredient present at a concentration $< 1\%$ can still be relevant for classifying the mixture for serious eye damage/eye irritation.”

Proposed amendments to address Item 5

Clarify in paragraphs 3.2.3.3.4 and 3.3.3.3.4 that care must be taken when classifying mixtures that contain the listed types of substances as opposed to taking care when classifying the substances themselves. And use the more consistently used term “substances” instead of “chemicals”.

Chapter 3.2

3.2.3.3.4 Amend as shown:

“3.2.3.3.4 Particular care must be taken when classifying mixtures containing certain types of ~~chemicals~~ substances such as acids and bases, inorganic salts, aldehydes, phenols, and surfactants. The approach explained in 3.2.3.3.1 and 3.2.3.3.2 might not work given that

many such substances are corrosive or irritant at concentrations < 1%. For mixtures containing strong acids or bases the pH should be used as classification criteria (see 3.2.3.1.2) since pH will be a better indicator of corrosion than the concentration limits in Table 3.2.3. 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 corrosion Category 1 if it contains \geq 1% of a corrosive ingredient and as skin irritation Category 2 or Category 3 when it contains \geq 3% of an irritant ingredient. Classification of mixtures with ingredients for which the approach in Table 3.2.3 does not apply is summarized in Table 3.2.4 below.”

Chapter 3.3

3.3.3.3.4 Amend as shown:

“3.3.3.3.4 Particular care must be taken when classifying mixtures containing certain types of chemicals substances such as acids and bases, inorganic salts, aldehydes, phenols, and surfactants. The approach explained in 3.3.3.3.1 and 3.3.3.3.2 might not work given that many such substances are seriously damaging to the eye/eye irritating at concentrations < 1%. For mixtures containing strong acids or bases the pH should be used as classification criterion (see 3.3.3.1.2) since pH will be a better indicator of serious eye damage (subject to consideration of acid/alkali reserve) than the concentration limits in Table 3.3.3. A mixture containing corrosive or serious eye damaging/eye irritating ingredients that cannot be classified based on the additivity approach applied in Table 3.3.3 due to chemical characteristics that make this approach unworkable, should be classified as Eye Category 1 if it contains \geq 1% of a corrosive or serious eye damaging ingredient and as Eye Category 2 when it contains \geq 3% of an eye irritant ingredient. Classification of mixtures with ingredients for which the approach in Table 3.3.3 does not apply is summarized in Table 3.3.4.”

Proposed amendments to address Item 6

Clarify the ambiguity in the last sentence in paragraphs 3.2.3.3.5 and 3.3.3.3.5.

Chapter 3.2

3.2.3.3.5 Amend as shown:

“3.2.3.3.5 On occasion, reliable data may show that the skin corrosion/irritation of an ingredient will not be evident when present at a level above the generic concentration limits/cut-off values mentioned in Tables 3.2.3 and 3.2.4. In these cases, the mixture could be classified according to those data (see also *Classification of hazardous substances and mixtures – Use of cut-off values/Concentration limits* (1.3.3.2)). On occasion, when it is expected that the skin corrosion/irritation of an ingredient will not be evident when present at a level above the generic concentration cut-off values mentioned in Tables 3.2.3 and 3.2.4, testing of the mixture may be considered. ~~In those cases, the tiered weight of evidence approach should be applied as described in 3.2.3 and illustrated in Figure 3.2.1.”~~

Chapter 3.3

3.3.3.3.5 Amend as shown:

“3.3.3.3.5 On occasion, reliable data may show that the irreversible/reversible eye effects of an ingredient will not be evident when present at a level above the generic cut-off values/concentration limits mentioned in Tables 3.3.3 and 3.3.4. In these cases, the mixture could be classified according to those data (see also 1.3.3.2 “*Use of cut-off values/Concentration limits*”). On occasion, when it is expected that the skin corrosion/irritation or the irreversible/reversible eye effects of an ingredient will not be evident when present at a level above the generic concentration/cut-off levels mentioned in Tables 3.3.3 and 3.3.4, testing of the mixture may be considered. ~~In those cases, the tiered~~

weight of evidence approach should be applied as referred to in section 3.3.3, Figure 3.3.1 and explained in detail in this chapter.”

Proposed amendments to address Item 7

Clarify the inconsistent terminology use in the following 3 cases:

1. Inconsistency in the last sentence of the Substantially similar bridging principle.
2. Use of the term “aerosol” at the beginning of the Aerosols bridging principle.
3. Inconsistency in the use of the term hazards vs. properties in paragraphs 3.2.3.3.1 and 3.3.3.3.1

1. Inconsistency in the last sentence of the Substantially similar bridging principle

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 can be ~~assigned~~ classified in the same hazard category.

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 serious eye damage/eye irritation 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 serious eye damage/eye irritation potential of B.

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

3.4.3.2.6 *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) 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 based on test data~~, then the other mixture can be ~~assigned~~ classified in the same hazard category.

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 based on test data~~, then the other mixture can be classified in the same hazard category.

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 based on test data~~, then the other mixture can be ~~assigned~~ classified in the same hazard category.

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 based on test data~~, then the other mixture can be ~~assigned~~ classified in the same hazard category.

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 based on test data~~, then the other mixture can be ~~assigned~~ classified in the same hazard category.

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 based on test data~~, then the other mixture can be ~~assigned~~ classified in the same hazard category.

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 can be ~~assigned~~ classified in the same hazard category.

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

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

2. Use of the term “aerosol” at the beginning of the Aerosols bridging principle

3.1.3.5.7 *Aerosols*

An ~~aerosol~~ aerosolised form of a mixture may be classified in the same hazard category as the tested, ~~non-aerosolized~~ non-aerosolised 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~~ aerosolised mixtures for inhalation toxicity should be considered separately.

3.2.3.2.7 *Aerosols*

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

3.3.3.2.7 *Aerosols*

An ~~aerosol~~ aerosolised form of a mixture may be classified in the same hazard category as the tested ~~non-aerosolized~~ non-aerosolised form of the mixture provided that the added propellant does not affect the serious eye damage/eye irritation properties of the mixture upon spraying.

3.4.3.2.7 *Aerosols*

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

3.8.3.3.7 *Aerosols*

An ~~aerosol~~ aerosolised form of a mixture may be classified in the same hazard category as the tested, ~~non-aerosolized~~ non-aerosolised 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~~ aerosolised mixtures for inhalation toxicity should be considered separately.

3.9.3.3.7 *Aerosols*

An ~~aerosol~~ aerosolised form of a mixture may be classified in the same hazard category as the tested, ~~non-aerosolized~~ non-aerosolised 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~~ aerosolised mixtures for inhalation toxicity should be considered separately.

3. Inconsistency in the use of the term hazards vs. properties in paragraphs 3.2.3.3.1 and 3.3.3.3.1

3.3.3.3.1 In order to make use of all available data for purposes of classifying the serious eye damage/eye irritation ~~properties~~ hazards of the mixtures, the following assumption has been made and is applied where appropriate in the tiered approach:

The “relevant ingredients” of a mixture are those which are present in concentrations $\geq 1\%$ (w/w for solids, liquids, dusts, mists and vapours and v/v for gases), unless there is a presumption (e.g. in the case of corrosive ingredients) that an ingredient present at a concentration $< 1\%$ can still be relevant for classifying the mixture for serious eye damage/eye irritation.

Proposed amendments to address Item 8

Clarify the inconsistent use of the:

- Terms hazard class vs. endpoint effects,
- Order of the terms “cut-off values” and “concentration limits”,
- Reference to the Section 1.3.3.2, and
- Reference to another paragraph and Figure in the paragraphs 3.2.3.3.5 and 3.3.3.3.5

Chapter 3.2

3.2.3.3.5 Amend as shown:

“3.2.3.3.5 On occasion, reliable data may show that the skin corrosion/irritation of an ingredient will not be evident when present at a level above the generic ~~concentration limits/cut-off values~~ cut-off values/concentration limits mentioned in Tables 3.2.3 and 3.2.4. In these cases, the mixture could be classified according to those data (~~see also Classification of hazardous substances and mixtures – Use of cut-off values/Concentration limits (1.3.3.2)~~ see also 1.3.3.2). On occasion, when it is expected that the skin corrosion/irritation of an ingredient will not be evident when present at a level above the generic ~~concentration cut-off values~~ cut-off values/concentration limits mentioned in Tables 3.2.3 and 3.2.4, testing of the mixture may be considered. In those cases, the tiered weight of evidence approach should be applied as ~~described in 3.2.3 and illustrated in Figure 3.2.1 referred to in section 3.2.3, Figure 3.2.1 and explained in detail in this chapter.~~”

Chapter 3.3

3.3.3.3.5 Amend as shown:

“3.3.3.3.5 On occasion, reliable data may show that the ~~irreversible/reversible eye effects~~ serious eye damage/eye irritation of an ingredient will not be evident when present at a level above the generic cut-off values/concentration limits mentioned in Tables 3.3.3 and 3.3.4. In these cases, the mixture could be classified according to those data (see also 1.3.3.2 ~~“Use of cut-off values/Concentration limits”~~). On occasion, when it is expected that the skin corrosion/irritation or the ~~irreversible/reversible eye effects~~ serious eye damage/eye irritation of an ingredient will not be evident when present at a level above the generic ~~concentration/cut-off levels~~ cut-off values/concentration limits mentioned in Tables 3.3.3 and 3.3.4, testing of the mixture may be considered. In those cases, the tiered weight of evidence approach should be applied as referred to in section 3.3.3, Figure 3.3.1 and explained in detail in this chapter.”

Proposed amendments to address Item 9

For consistency, update the hazard communication section of each physical, health and environmental chapter to refer to the label elements table

Chapter 2.1

2.1.3 Amend as shown:

“2.1.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.1.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter. “

Chapter 2.2

2.2.3.1 Amend as shown:

“2.2.3.1 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.2.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 2.3

2.3.1.3 Amend as shown:

“2.3.1.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.3.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

2.3.2.3 Amend as shown:

“2.3.2.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.3.4

presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 2.4

2.4.3 Amend as shown:

“2.4.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.4.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 2.5

2.5.3 Amend as shown:

“2.5.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.5.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 2.6

2.6.3 Amend as shown:

“2.6.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.6.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter. “

Chapter 2.7

2.7.3 Amend as shown:

“2.7.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.7.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 2.8

2.8.3 Amend as shown:

“2.8.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.8.1 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 2.9

2.9.3 Amend as shown:

“2.9.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.9.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 2.10

2.10.3 Amend as shown:

“2.10.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.10.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 2.11

2.11.3 Amend as shown:

“2.11.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.11.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 2.12

2.12.3 Amend as shown:

“2.12.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.12.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 2.13

2.13.3 Amend as shown:

“2.13.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.13.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 2.14

2.14.3 Amend as shown:

“2.14.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.14.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 2.15

2.15.3 Amend as shown:

“2.15.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.15.1 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 2.16

2.16.3 Amend as shown:

“2.16.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.16.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 2.17

2.17.3 Amend as shown:

“2.17.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 2.17.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 3.1

3.1.4.1 Amend as shown:

“3.1.4.1 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. ~~The table below presents specific label elements for substances and mixtures that are classified into acute toxicity hazard categories 1 to 5 based on the criteria set forth in this chapter.~~ Table 3.1.3 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 3.2

3.2.4 Amend as shown;

“3.2.4 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. ~~The table below presents specific label elements for substances and mixtures that are classified as irritating or corrosive to the skin based on the criteria set forth in this chapter.~~ Table 3.2.5 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 3.3

3.3.4 Amend as shown:

“3.3.4 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 3.3.5 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 3.4

3.4.4.1 Amend as shown:

“3.4.4.1 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. ~~Table 3.4.6 below presents specific label elements for substances and mixtures that are classified as respiratory and skin sensitizers based on the criteria in this chapter.~~ Table 3.4.6 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 3.5

3.5.4 Amend as shown:

“3.5.4 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. ~~The table below presents specific label elements for substances and mixtures classified as germ cell mutagens based on the criteria in this chapter.~~ Table 3.5.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 3.6

3.6.4 Amend as shown:

“3.6.4 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and

pictograms which can be used where allowed by the competent authority. ~~Table 3.6.2 below presents specific label elements for substances and mixtures that are classified as carcinogenic based on the criteria set forth in this chapter.~~ Table 3.6.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 3.7

3.7.4 Amend as shown:

“3.7.4 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 3.7.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 3.8

3.8.4.1 Amend as shown:

“3.8.4.1 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 3.8.3 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 3.9

3.9.4 Amend as shown:

“3.9.4 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Table 3.9.4 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 3.10

3.10.4.1 Amend as shown:

“3.10.4.1 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. ~~The table below presents specific label elements for substances and mixtures which are classified as posing an aspiration toxicity hazard, Categories 1 and 2, based on the criteria set forth in this chapter.~~ Table 3.10.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 4.1

4.1.4 Amend as follows:

“4.1.4 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Tables 4.1.6 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”

Chapter 4.2

4.2.3 Amend as shown:

“4.2.3 General and specific considerations concerning labelling requirements are provided in Hazard communication: Labelling (Chapter 1.4). Annex 1 contains summary tables about classification and labelling. Annex 3 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Tables 4.2.2 presents specific label elements for substances and mixtures classified into this hazard class based on the criteria in this chapter.”
