

## **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 of Classification  
and Labelling of Chemicals)**

### **Status report and proposal 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 provides an update on the work undertaken by the Practical Classification Issues (PCI) informal correspondence group since the December 2021 Sub-Committee meeting and also includes proposals to address issues from the PCI program of work.

#### **Status report**

2. The PCI has had four web conferencing meetings since the December Subcommittee meeting. The group has been focused on Issues (f), the tiered approach for classifying mixtures in chapters 3.2 to 3.4, and Issue (g), address the issues referred to the PCI from the Non-Animal Test Methods Informal Working Group (NATM WG). The PCI will continue to schedule a series of virtual meetings after the July session to further progress items from the program of work.

#### **Proposal to address issues from the program of work**

3. The PCI has made significant progress working the items referred to the PCI from the NATM WG and has reached consensus on a path forward for 7 of the 9 items. The NATM WG description of items referred to the PCI are provided in Annex 1 for reference. Annex 2 provides proposals that address the issues raised for Items 1, 4, 5, 6, 8 and 9. With regard to Item 3, the group decided to pause work on this item pending further work on PCI Program of Work Issue (f). The remaining 2 items (i.e., Item 2 and 7) will be discussed in upcoming virtual meetings.

4. The PCI invites the Sub-Committee to consider the recommended editorial amendments to the GHS as set forth in Annex 2 of this document. Input from the Sub-Committee will be incorporated into a formal paper for the December 2022 meeting.

## Annex 1

### Work item (g) from the PCI Program of Work (INF.31, 39<sup>th</sup> session)

Develop proposals, as appropriate, to address technical errors and/or editorial improvements referred by the non-animal test methods informal working group.

#### Items referred to the PCI from the NATM WG

**1. The use of the term ‘Weight of Evidence (WoE) approach’ vs ‘WoE assessment’**

These terms are both used within the purple book although they probably have the same meaning. The NATM IWG proposes to only use the term ‘WoE assessment’ for clarity and consistency reasons and will propose adaption of chapter 3.2 and 3.3 as this is within their mandate. However, different terms such as WoE assessment/approach/determination/evaluation/analysis are also used outside chapter 3.2 and 3.3. Therefore, it is suggested to discuss within the PCI whether the other chapters can be adapted in the same way to make the purple book consistent.

**2. The use of the term ‘elements may be relevant’**

The term ‘not all elements may be relevant’ is included in chapter 3.2 (3.2.2.7.1) and 3.3 (3.3.2.10.1 and 3.3.5.3.4.2) in relation to the tiered approach but the meaning of “elements” (tiers? elements within a tier? both?) and “relevant” (available? considered? applicable? appropriate? important?) was considered unclear. A similar term is also used in chapter 4.1.3.2 in relation to the tiered approach. It is suggested to discuss the intention of this term and to adapt it when necessary.

**3. Paragraphs 3.2.3.2.1, 3.3.3.2.1 and similar paragraphs**

Paragraphs 3.2.3.2.1 and 3.3.3.2.1 contain the wording ‘Where the mixture itself has not been tested to determine its ...’. The same wording is also used in other chapters. However, a conclusion for the mixture could also be based on human experience, *in silico* methods or other non-testing data. Therefore, it was suggested to adapt this sentence for example with ‘Where the mixture itself has no conclusive information to decide on its ...’. It is suggested to discuss the potential revision of this paragraph in all chapters.

**4. Paragraphs 3.2.3.3.1 and 3.3.3.3.1**

Paragraphs 3.2.3.3.1 and 3.3.3.3.1 contain the wording ‘the following assumption has been made and is applied where appropriate in the tiered approach:’. This is considered slightly confusing as it can be mistakenly associated with the tiered approach to substances described in Figures 3.2.1 and 3.3.1. It is proposed to revise the sentence to: ‘the following assumption has been made and is applied where appropriate in the tiered approach to mixtures (see 1.3.2.3 and 1.3.3):’. It is suggested to discuss the proposed sentence.

**5. Paragraphs 3.2.3.3.4 and 3.3.3.3.4**

Both paragraphs contain the sentence ‘Particular care must be taken when classifying certain types of chemicals such as acids and bases, inorganic salts, aldehydes, phenols, and surfactants’, which was not considered correct because the sentence actually refers to the classification of mixtures containing this type of substances and not classification of the substances themselves. The following suggestion was made: ‘Particular care must be taken when classifying mixtures containing certain types of substances such as acids and bases, inorganic salts, aldehydes, phenols, and surfactants.’ It is suggested to discuss the proposed sentence.

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**6. Paragraphs 3.2.3.3.5 and 3.3.3.3.5**

In the last sentence the wording ‘In those cases’ was considered unclear as this could be read as referring to testing as stated in the sentence before. It was suggested to replace the wording with ‘Where new testing data become available’. We suggest to discuss the proposed change.

**7. Paragraphs 3.3.3.2.6, 3.3.3.2.7 and 3.3.3.3.1**

The paragraphs slightly differ from the corresponding paragraphs for skin irritation/corrosion (3.2.3.2.6, 3.2.3.2.7 and 3.2.3.3.1). It is suggested to review whether these differences were introduced on purpose and to consider aligning the text if justified. Other chapters could be checked for additional differences. In 3.3.3.2.7, “An aerosol form of a mixture ” the beginning of the paragraph could be revised to “An aerosolised form of a mixture” to align with the same term used later in the same sentence.

**8. Paragraph 3.3.3.3.5 versus 3.2.3.3.5**

These paragraphs slightly differ regarding the use of the wording irreversible/reversible eye effect in chapter 3.3 versus the wording skin corrosion/irritation in chapter 3.2. In fact, this is the only paragraph in the whole 3.3.3 section where “irreversible/reversible eye effects” is used instead of “serious eye damage/eye irritation”. It is suggested to review whether these differences were introduced on purpose and to consider aligning the text if justified. Other minor differences in this paragraph between the chapters 3.2 and 3.3 could also be aligned.

**9. Paragraph 3.3.4**

This paragraph misses the sentence “The table below presents specific label elements for substances and mixtures that are classified as serious eye damage or eye irritant based on the criteria set forth in this chapter.” as included in chapter 3.2.4 (for “irritating or corrosive to the skin”). It is suggested to review whether these differences were introduced on purpose and to consider aligning the text if justified. The consistency with other chapters could be checked.

## Annex 2

### Proposed editorial revisions to the GHS

#### Work Item (g) from the PCI Program of Work (UN/SCEGHS/39/INF.31):

Develop proposals, as appropriate, to address technical errors and/or editorial improvements referred by the Non-Animal Test Methods Informal Working Group.

**Issue 1 For consistency, review the different terms WoE approach/determination/evaluation/ analysis throughout the GHS, and where appropriate revise the text to WoE assessment. However, during the review it was acknowledged that in some cases the term WoE approach is more appropriate due to the context and intention. Therefore, these cases are not included in the proposals below.**

The proposed updates are indicated using ~~strikeout~~ and underline font.

#### 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 LD<sub>50</sub> 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.”

## 3.4.2.2.1.3 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.”

## 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:

*<sup>a</sup> 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.*

*<sup>b</sup> 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.”

3.9.2.10 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 values<sup>1</sup>. 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”. 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.”

**Issue 4 In paragraphs 3.2.3.3.1 and 3.3.3.3.1, it is not clear that the use of the term “tiered approach” is referring to the mixture tiered approach vs. the substance tiered approach**

The proposed updates are indicated using ~~strikeout~~ and underline font.

**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 ~~and 1.3.3~~):

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 ~~and 1.3.3~~):

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.”

**Issue 5 In paragraphs 3.2.3.3.4 and 3.3.3.3.4, clarify 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. Also, replace the use of the term “chemicals” with the more consistently used term “substances”**

The proposed updates are indicated using ~~strikeout~~ and underline font.

**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 ≥ 1% of a corrosive or serious eye damaging ingredient and as Eye Category 2 when it contains ≥ 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.”

**Issue 6**    **In paragraphs 3.2.3.3.5 and 3.3.3.3.5, it is not clear in the last sentence what “In those cases” is referring to in the paragraph. Thus provide an editorial revision to provide clarity**

The proposed updates are indicated using ~~strikeout~~ and underline font.

**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.”~~

**Issue 8** In paragraphs 3.2.3.3.5 and 3.3.3.3.5, there are 4 types of inconsistencies regarding terminology (e.g., hazard class vs. endpoint effects, order of the terms cut-off value and concentration limits, reference to section 1.3.3.2 and reference to another paragraphs and figure) which are addressed

The proposed updates are indicated using ~~strikeout~~ and underline font.

## 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.”

**Issue 9** In the hazard communication section of each physical, health and environmental chapter the last sentence before the table with the label elements is not consistent throughout the GHS

The proposed updates are indicated using ~~strikeout~~ and underline font.

## 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”

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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~~ 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.”

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