INFORMATION PAPER ON AGENDA ITEM 4

PROPOSALS FOR MODIFICATION OF THE DRAFT GHS-DOCUMENT

Transmitted by the experts from Belgium, Austria, Finland, Norway, Sweden and the United Kingdom

Issues that are part of OECD Integrated Document but not included in the draft GHS Document


Add "See chapter 1.2, paragraph 17" after the text "Positive data from experimental studies from man".


"The proceedings of a WHO/IPCS working group on harmonised risk assessment for carcinogenicity points to a number of scientific questions arising for classification of chemicals e.g. mouse liver tumours, peroxisome proliferation, receptor-mediated reactions, chemicals which are carcinogenic only at toxic doses and which do not demonstrate mutagenicity. Accordingly, there is a need to articulate the principles necessary to resolve these scientific issues, which have led to diverging classifications in the past. Once these issues are resolved, there would be a firm foundation for classification of a number of chemical carcinogens."


Add a new paragraph after paragraph 6 of Annex 12, Carcinogenicity, page 13:

"Considerations for important factors mentioned in Chapter 3.6 paragraph 9"

Guidance on the importance of the different factors mentioned in paragraph 9 of chapter 3.6 has to be developed in order to indicate their effects or level of concern."


ST/SG/AC.10/C.4/2001/23, page 27, Chapter 3.7, Paragraph 5, third line and second box, replace word 'class' by word 'category'.


Proposals to improve the ‘Guidance text’ of draft GHS-Document


ST/SG/AC.10/C.4/2001/28, Annex 12, page 11, add a new paragraph after paragraph 2:

"Acute toxicity

The criteria for acute toxicity should be revised to take account of new test methods replacing the LD50-method."


Replace in ST/SG/AC.10/C.4/2001/28, Annex 12 on page 13 the subheading ‘Classification of mixtures containing substances having effects on or via lactation’ by ‘Classification of substances and mixtures having effects on or via lactation’.

Add in the beginning of paragraph 5.1 under subheading ‘Classification of substances and mixtures having effects on or via lactation.’ a sentence “Examine whether a separate class is needed for lactation effects.”

Add a new paragraph in Annex 12, page 13, after paragraph 5.1:

"Terminology

The terms "reproductive toxicity", "developmental toxicity" and "reproductive ability and capacity" used in paragraphs 5 and 6 of chapter 3.7 (Document ST/SG/AC.10/C.4/2001/23, page 26 - 27) should be clarified."
Proposal for modification of Decision Logic schemes, documents
ST/SG/AC.10/C.4/2001/22, page 15,
ST/SG/AC.10/C.4/2001/22, page 31,
ST/SG/AC.10/C.4/2001/22, page 46,
ST/SG/AC.10/C.4/2001/22, page 58,
ST/SG/AC.10/C.4/2001/22, page 60,
ST/SG/AC.10/C.4/2001/23, page 9,
ST/SG/AC.10/C.4/2001/23, page 20,
ST/SG/AC.10/C.4/2001/23, page 35,
ST/SG/AC.10/C.4/2001/23, page 48,
ST/SG/AC.10/C.4/2001/23, page 61,


The footnote indicating a guidance nature of the Decision Logic schemes is proposed to be replaced by a text to be added in front of each Decision Logic scheme as a header. Following text is proposed:

"The decision logic which follows is not part of the harmonised classification system, but has been provided here as additional guidance only. The responsible person for classification is strongly recommended to study the criteria before and during use of the decision logic."

Chapter 3.2: Skin corrosion/irritation

- Footnote 3 is deleted and replaced by a corresponding header under the heading.
- The flowsheet is modified following the same model as for acute toxicity

- References to paragraphs of criteria are added in boxes for 'corrosive', 'irritant' and 'mild irritant'
- The word 'material' is replaced by 'substance' and 'mixture'
- The wording of boxes for 'corrosive', 'irritant' and 'mild irritant' is modified to correspond better to wording of criteria.

- Heading for Decision Logic 2 is added
- The information of boxes listing example substances and cases, where 'additivity' does not apply, are merged

ST/SG/AC.10/C.4/2001/22, page 34
- The cases where additivity does not apply and additivity applies are linked in the flowsheet
- In boxes, where summation formula are presented, a reference to specific concentration limits is introduced.

Chapter 3.3: Serious eye damage/Eye irritation

ST/SG/AC.10/C.4/2001/22, page 46
- Footnote 5 is deleted and replaced by a corresponding header under the heading.
• The flowsheet is modified following the same model as for acute toxicity

ST/SG/AC.10/C.4/2001/22, page 47
• References to paragraphs of criteria are added in boxes for 'irreversible eye damage', 'eye irritant' and 'mild irritant'
• The word 'material' is replaced by 'substance' and 'mixture'
• The wording of boxes for 'irreversible eye damage', 'eye irritant' and 'mild irritant' is modified to correspond better to wording of criteria.

• Heading for Decision Logic 2 is added
• The information of boxes listing example substances and cases, where 'additivity' does not apply, are merged

• The cases where additivity does not apply and additivity applies are linked in the flowsheet

Chapter 3.4: Respiratory or Skin Sensitisation

ST/SG/AC.10/C.4/2001/22, page 58 and 60
• Footnotes 6 and 8 are deleted and replaced to the top of the page under the heading

• The scheme starts with “Substance” instead of “Mixture”.
• The wording of the criteria in the box with the two bullets is amended to give the correct wording of the criteria.
• References to paragraphs in the criteria are introduced in relevant boxes.

ST/SG/AC.10/C.4/2001/22, page 60
• The scheme starts with “Substance” instead of “Mixture”.
• References to paragraphs in the criteria are introduced in relevant boxes.

Chapter 3.5: Germ Cell Mutagenicity

• Footnote 1 is deleted and replaced to the top of the page under the heading.

Substance:
• Changes made in the texts of first, second and third vertical box.

Mixture:
• Page 10: The part of the flowsheet on classification based on data for the mixture as a whole or bridging principles has been changed to a footnote in the new DL on mixtures. Left from the previous version is the first, upper box on Mixture (text slightly modified), followed by the flowsheet on classification based on individual ingredients of the mixture, on page 11.

Chapter 3.6: Carcinogenicity

• Footnote 1 is deleted and replaced to the top of the page under the heading.
Substance:
- Changes made in the texts of first, second and third vertical box

Mixture:
- Page 21: The part of the flowsheet on classification based on data for the mixture as a whole or bridging principles has been changed to a footnote in the new DL on mixtures. Left from the previous version is the first, upper box on Mixture (text slightly modified), followed by the flowsheet on classification based on individual ingredients of the mixture, on page 22. A deletion “See table of this chapter for explanation of cut-off values/concentration limits” is made in the text of the second vertical box on page 22.

Chapter 3.6: Reproductive toxicity

- Footnote 1 is deleted and replaced to the top of the page under the heading

Substance:
- Changes made in the texts of first, second and third vertical box

Mixture:
- Page 37-38: The part of the flowsheet on classification based on data for the mixture as a whole or bridging principles has been changed to a footnote in the new DL on mixtures. Left from the previous version is the first, upper box on Mixture (text slightly modified), followed by the flowsheet on classification based on individual ingredients of the mixture, on page 38. A deletion “See table 1 of this chapter for explanation of cut-off values/concentration limits” is made in the text of the second and third vertical box on page 38.

Chapter 3.8: Specific target organ systemic toxicity - Single exposure

- The flowsheet is modified following the same model as for acute toxicity
- The wording of boxes is modified to emphasise better the criteria.
- References to paragraphs of criteria are added in boxes.
- Reference to 'expert judgement' and 'weight of evidence' is placed as the last sentence in the box.

Chapter 3.8: Specific target organ systemic toxicity - Repeated exposure

- The flowsheet is modified following the same model as for acute toxicity
- The wording of boxes is modified to emphasise better the criteria.
- References to paragraphs of criteria are added in boxes.
- Reference to 'expert judgement' and 'weight of evidence' is placed as the last sentence in the box.

Chapter 3.10: Hazardous to the aquatic environment

ST/SG/AC.10/C.4/2001/23, p. 79
- The heading is changed from 'Decision logic and guidance' to 'Decision logic'.
- Footnote 1 is deleted and replaced by a corresponding header under the heading.

• The first bullet point of the second Chronic box "Is it poorly soluble with no acute toxicity up to the water solubility," has been changed in the following way:

“Is it poorly soluble with no acute toxicity* up to the water solubility,…”

And the added footnote say:

* See Table 1, Note 5 further developed in Annex 9, paras 66 and 67.
ST/SG/AC.10/C.4/2001/23, p. 82-83

• Wherever the M factor is included a footnote has been added to say:

*For explanation of the M factor see paragraph 56.

Miscellaneous

The relevant paragraph numbers for detailed explanation of criteria should be used consistently in all decision logic and guidance schemes (e.g. see sensitisation).

The numbering and references of footnotes in the final text has to be re-checked.

Reprinted modified Decision Logic schemes are attached.
Replace the Decision Logic for skin corrosion irritation by the following:

**Decision Logic for skin corrosion/irritation**

The decision logic, which follows is not part of the harmonised classification system, but has been provided here as additional guidance (only). The responsible person for classification is strongly recommended to study the criteria before and during use of the decision logic.

**Decision Logic 1**

**Substance**: Are there data/information to evaluate skin corrosion/irritation?

- **No**: Classification not possible

- **Yes**:  
  
  **Mixture**: Does the mixture as whole or its ingredients have data/information to evaluate skin corrosion/irritation?
  
  - **No**: Classification not possible
  
  - **Yes**: See Decision Logic 2 for use with ingredients

**Is the substance or mixture corrosive** (see paragraphs 1, 4-8 and 14) considering:
- Existing human experience showing irreversible damage to skin,
- Existing animal observations indicating skin corrosion after single exposure,
- In vitro data,
- Information available from structurally related compounds,
- pH extremes of ≤ 2 or ≥ 11.5, including consideration of acid/alkali reserve capacity, if appropriate
- Destruction of skin in 1 or more test animals. (see paragraph 8 Table 1 for criteria and sub-categorisation)

- **Yes**: Category 1

**Danger**

Continued Next Page
Is the **substance or mixture** an irritant (see paragraphs 2, 4-6 and 9-12) considering:
- Existing human experience and data, single or repeated exposure
- Existing animal observations including single or repeated exposure,
- In vitro data,
- Information available from structurally related compounds,
- Skin irritation data from an animal study (See paragraph 12 Table 2 for criteria)

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3 Figure 1 contains details for testing and evaluation.
Decision Logic 2 Classification of mixtures on the basis of information/data on ingredients

Can bridging principles be applied (see paragraphs 15-21)?

Yes

Classify in appropriate category

No

Does the mixture contain ≥ 1% ingredients (or where relevant < 1%, see paragraph 22, and for specific concentration limits, see chapter 1.2 paragraphs 28-30) which are corrosive (see paragraphs 1, 4-8) and for which additivity principle may not apply, such as:
- Acids and bases with extreme pH's ≤ 2 or ≥ 11.5, including consideration of acid/alkali reserve capacity, if appropriate, or
- Inorganic salts, or
- Aldehydes, or
- Phenols, or
- Surfactants, or
- Other ingredients?

Yes

Category 1
Danger

No

Does the mixture contain ≥ 3% (for specific concentration limits, see chapter 1.2 paragraphs 28-30) of 4 ingredients which are irritant (see paragraphs 4-6, 9-12) and for which additivity principle may not apply, including acids and bases?

Yes

Category 2
Warning

No

4 See Chapter 1.2 for “The Use of Cut-off Values/Concentration Limits” as well as paragraph 27 of this chapter.
Does additivity principle apply?

Yes

Sum of concentrations of ingredients classified as\(^5\):  
I. Skin Category 1 ≥ 5%?  
(for specific concentration limits, see chapter 1.2. paragraphs 28-30)

No

Sum of concentrations of ingredients classified as\(^5\):  
II. Skin Category 1 ≥ 1% but ≤ 5%, or  
III. Skin Category 2 ≥ 10%, or  
IV. (10 x Skin Category 1) + Skin Category 2 ≥ 10%?  
(for specific concentration limits, see chapter 1.2. paragraphs 28-30)

No

Sum of concentrations of ingredients classified as\(^5\):  
V. Skin Category 2 ≥ 1% but ≤ 10%, or  
VI. Skin Category 3 ≥ 10%, or  
VII. (10 x Skin Category 1) + Skin Category 2 ≥ 1% but ≤ 10%, or  
VIII. (10 x Skin Category 1) + Skin Category 2 + Skin Category 3 ≥ 10%?  
(for specific concentration limits, see chapter 1.2. paragraphs 28-30)

No

Not classified

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\(^5\) See Chapter 1.2 for “The Use of Cut-off Values/Concentration Limits” as well as paragraph 27 of this chapter.

\(^6\) See note to Table 3 for details on use of Category 1 subcategories.
Replace the Decision Logic for serious eye damage/eye irritation by the following:

**Decision Logic for serious eye damage/ eye irritation:**

The decision logic, which follows is not part of the harmonised classification system, but has been provided here as additional guidance only. The responsible person for classification is strongly recommended to study the criteria before and during use of the decision logic.

**Decision Logic 1**

**Substance:** Are there data/information to evaluate serious eye damage/eye irritation?

- **Yes**
  - **Mixture:** Does the mixture as a whole or its ingredients have data/information to evaluate serious eye damage/ eye irritation?
    - **Yes**
      - **Mixture:** Does the mixture as a whole have data/information to evaluate serious eye damage/ eye irritation?
        - **Yes**
          - Does the substance or mixture have potential to cause irreversible eye damage (serious eye damage, see paragraphs 1 and 5 - 11) considering:
            - Existing human experience,
            - Existing animal observations including single or repeated exposure,
            - In vitro data,
            - Information available from structurally related compounds,
            - pH extremes of ≤ 2 or ≥ 11.5, including consideration of acid/alkali reserve capacity, if appropriate
            - Irreversible eye damage in 1 or more test animals.
            (see paragraph 11 Table 1 for criteria and sub-categorization)

    - **No**
      - See Decision Logic 2 for use with ingredients
  - **No**
    - Classification not possible

- **No**
  - Classification not possible

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Is the **substance or mixture** an eye irritant (see paragraphs 2, 5-10 and 12-14) considering:
- Existing human experience and data, single or repeat exposure
- Existing animal observations including single or repeated exposure,
- In vitro data,
- Information available from structurally related compounds,
- Eye irritation data from an animal study (See paragraph 13 Table 2 for criteria for category 2A)

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5 Figure 1 contains details for testing and evaluation.
Decision Logic 2 Classification of mixtures on the basis of information/data on ingredients

Can bridging principles be applied (see paragraph 17-23)?

Yes

Classify in appropriate category

No

Does the mixture contain ≥ 1 % (for specific concentration limits, see chapter 1.2 paragraphs 28-30) of ingredients which cause irreversible eye damage (see paragraphs 10 and 12-14) and for which additivity principle may not apply, such as:

- Acids and bases with extreme pH's ≤ 2 or ≥ 11.5, including consideration of acid/alkali reserve capacity,
- Inorganic salts, or
- Aldehydes, or
- Phenols, or
- Surfactants, or
- Other ingredients?

Yes

Category 1

Danger

No

Does the mixture contain ≥ 3% (see chapter 1.2 paragraphs 28-30 for specific concentration limits) of ingredients which are irritant (see paragraphs 10 and 12-14) and for which additivity principle may not apply, including acids and bases?

Yes

Category 2

Warning

No

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6 See Chapter 1.2 for “The Use of Cut-Off Values/Concentration Limits”, as well as paragraphs 24-29.
7 See Chapter 1.2 for “The Use of Cut-off Values/Concentration Limits”, as well as paragraphs 24-29 of this Chapter.
Replace the Decision Logic for Classification of Dermal Sensitisation by the following:

**Decision Logic for Classification of Dermal Sensitisation**

The decision logic, which follows is not part of the harmonised classification system, but has been provided here as additional guidance only. The responsible person for classification is strongly recommended to study the criteria before and during use of the decision logic.

1 See “The use of Cut-off Values/Concentration Limits” in Chapter 1.2.
Replace the Decision Logic for Classification of Respiratory Sensitisation by the following:

**Decision Logic for Classification of Respiratory Sensitisation**

The decision logic, which follows is not part of the harmonised classification system, but has been provided here as additional guidance only. The responsible person for classification is strongly recommended to study the criteria before and during use of the decision logic.

1. **Substance:** Does the substance have respiratory sensitisation data?
   - No: Classification not possible
   - Yes: Mixture:
     - Does the mixture as a whole have respiratory sensitisation data? (see remark in paragraph 19)

     1. Is there evidence in humans that the substance/mixture can induce specific respiratory hypersensitivity, and/or
     2. are there positive results from an appropriate animal test? (see criteria in paragraphs 3-9)

     1. Yes: Category 1
        - New Symbol
        - Danger
     2. No: Can bridging principles be applied? (see paragraphs 20-24)

     - Yes: Not classified
     - No: Does the mixture contain one or more ingredients classified as a respiratory sensitzer at 1:
       - ≥ 1% w/w (solid/liquid), or
       - ≥ 0.2% v/v (gas)? (see paragraph 25)

     - Yes: Category 1
        - New Symbol
        - Danger
     - No: Not classified

1) See “The use of Cut-off Values/Concentration Limits” in Chapter 1.2
Replace the Decision Logic for the Classification of Germ Cell Mutagenicity by the following:

**Decision Logic for the Classification of Germ Cell Mutagenicity**

The decision logic, which follows is not part of the harmonised classification system, but has been provided here as additional guidance only. The responsible person for classification is strongly recommended to study the criteria before and during use of the decision logic.

**Substance:** Does the substance have data on mutagenicity?

- **No** → Classification not possible

- **Yes**

  Is the substance according to the criteria (see paragraphs 5-14):

  - **Known** to induce heritable mutations in germ cells of humans, or
  - **Should it be regarded** as if it induces heritable mutations in the germ cells of humans?

  Application of the criteria needs expert judgment in a weight of evidence approach

- **No** →

  Does the substance according to the criteria (see paragraphs 5-14) cause concern for humans owing to the possibility that it **may induce** heritable mutations in the germ cells of humans?

  Application of the criteria needs expert judgment in a weight of evidence approach.

- **Yes** → Category 1

  New Symbol

  Danger

- **No** → Category 2

  New Symbol

  Warning

- **No** → Not classified
Note on the applications of the mutagenic properties of a chemical for its potential classification as a carcinogen

It is increasingly accepted that the process of chemical-induced tumorigenesis in man and animals involves genetic changes in proto-oncogenes and/or tumour suppressor genes of somatic cells. Therefore, the demonstration of mutagenic properties of chemicals in somatic and/or germ cells of mammals in vivo may have implications for the potential classification of these chemicals as carcinogens (see also Carcinogenicity, Chapter 3.6, paragraph 10)

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22 See text for detailed criteria on subclasses
3 See “The use of Cut-off Values/Concentration Limits” in Chapter 1.2 and Table 1 of this Chapter
4 The classification may sometimes be modified on a case by case basis on the available test data for the mixture as a whole. If bridging principles will be applied, classify in the same category as the similar mixture. See criteria for further details
5 The text which follows is not part of the agreed text on the harmonised classifications system developed by the OECD Task Force-HCL, but has been provided here as additional guidance.
Replace the Decision Logic for Classification of Carcinogenicity by the following:

**Decision Logic for Classification of Carcinogenicity**

The decision logic, which follows is not part of the harmonised classification system, but has been provided here as additional guidance only. The responsible person for classification is strongly recommended to study the criteria before and during use of the decision logic.

- **Substance:** Does the substance have carcinogenicity data?
  - **No** Classification not possible
  - **Yes**
    - Is the substance according to the criteria (paragraphs 3-15):  
      - **Known** to have carcinogenic potential for humans, or
      - **Presumed** to have carcinogenic potential for humans;
    
      Application of the criteria needs expert judgment in a strength and weight of evidence approach
    
    - **Yes**
      - Category 1
        - New Symbol: Danger
    
    - **No**
      - Is the substance according to the criteria (paragraphs 3-15) a suspected human carcinogen?
        - Application of the criteria needs expert judgment in a strength and weight of evidence approach.
        - **Yes**
          - Category 2
            - New Symbol: Warning
        - **No**
          - Not classified
**Mixture:** Classification of mixtures will be based on the available test data for the individual ingredients of the mixture, using cut-off values/concentration limits for those ingredients, see paragraphs 16-21.\(^3,4\)

Does the mixture contain one or more ingredients classified as a Category 1 carcinogen at:
- \(\geq 0.1\%\)\(^3\)?

- **Yes**
  - Category 1\(^2\)
  - New Symbol
  - Danger

- **No**

Does the mixture contain one or more ingredients classified as a Category 2 carcinogen at:
- \(\geq 0.1\%\)\(^3\)?
- \(\geq 1.0\%\)\(^3\)?

- **Yes**
  - Category 2
  - New Symbol
  - Warning

- **No**

\(^2\) See text for detailed criteria on subclasses.

\(^3\) See “The use of Cut-off Values/Concentration Limits” in Chapter 1.2 and in Table 1 of this Chapter.

\(^4\) The classification may sometimes be modified on a case by case basis on the available test data for the mixture as a whole. If bridging principles will be applied, classify in the same category as the similar mixture. See criteria for further details.
Replace the Decision Logic for Classification of Reproductive Toxicity by the following:

**Decision Logic for Classification of Reproductive Toxicity**

The decision logic, which follows is not part of the harmonised classification system, but has been provided here as additional guidance only. The responsible person for classification is strongly recommended to study the criteria before and during use of the decision logic.

**Substance:** Does the substance have data on reproductive toxicity?

- **No**
  - Classification not possible

- **Yes**
  - Is the substance according to the criteria (paragraphs 5-27):
    - **Known** to have produced an adverse effect on reproductive ability or capacity, or on development, in humans, or
    - **Presumed** to produce an adverse effect on reproductive ability or capacity, or on development, in humans?

  Application of the criteria needs expert judgement in a weight of evidence approach.

- **No**
- **Yes**
  - Category 1
    - New Symbol
    - Danger

  Is the substance according to the criteria (see paragraphs 5-27) **suspected** to produce an adverse effect on reproductive ability or capacity, or on development, in humans?

  Application of the criteria needs expert judgement in a weight of evidence approach.

- **No**
- **Yes**
  - Category 2
    - New Symbol
    - Warning

  Not classified as reproductive toxicant

**Decision logic for effects on or via lactation:**

Does the substance according to the criteria (see paragraphs 5-27) cause concern for the health of breastfed children?

- **No**
- **Yes**
  - Additional category for effects on or via lactation

  Not classified in additional category
**Mixture:** Classification of mixtures will be based according to the criteria (paragraphs 28-33) on the available test data for the individual ingredients of the mixture, using cut-off values/concentration limits for those ingredients.

Does the mixture contain one or more ingredients classified as a Category 1 reproductive toxicant at:
- $\geq 0.1\%$?

- **Yes**
  - Category 1
  - New Symbol
  - Danger

- **No**

Does the mixture contain one or more ingredients classified as a Category 2 reproductive toxicant at:
- $\geq 0.1\%$?
- $\geq 1.0\%$?

- **Yes**
  - Category 2
  - New Symbol
  - Warning

- **No**
  - Not classified

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2 See text for detailed criteria on subclasses.
3 See “The use of Cut-off Values/Concentration Limits” in Chapter 1.2 and in Table 1 of this Chapter.
4 The classification may sometimes be modified on a case by case basis on the available test data for the mixture as a whole. If bridging principles will be applied, classify in the same category as the similar mixture. See criteria for further details.
Replace the Decision Logic for Target Organ Systemic Toxicity from single exposure by the following:

**Decision Logic for Target Organ Systemic Toxicity from Single Exposure**

The decision logic, which follows is not part of the harmonised classification system, but has been provided here as additional guidance only. The responsible person for classification is strongly recommended to study the criteria before and during use of the decision logic.

**Substance:** Does the substance have data and/or information to evaluate target organ systemic toxicity following single exposure?

- **No** Classification not possible

**Mixture:** Does the mixture as a whole or its ingredients have data/information to evaluate target organ systemic toxicity following single exposure?

- **No** Classification not possible
- **Yes** Does the mixture as a whole have data/information to evaluate target organ systemic toxicity following single exposure?
  - **No** See Decision Logic 2
  - **Yes**

**Following single exposure**
- Can the substance or mixture produce significant toxicity in humans, or can it be presumed to have the potential to produce significant toxicity in humans on the basis of evidence from studies in experimental animals?

See paragraphs 7-27 for criteria and guidance values. Application of the criteria needs expert judgment in a weight of evidence approach.

**Following single exposure**
- can the substance or mixture, be presumed to have the potential to be harmful to human health on the basis of evidence from studies in experimental animals?

See paragraphs 7-25 for criteria and guidance including values. Application of the criteria needs expert judgment in a weight of evidence approach.

**No**

**New Symbol**
- **Category 1** Danger
- **Category 2** Warning

**Not classified**

*Continued on next page*
Decision logic 2

Can bridging principles, paragraphs 28-34 be applied?

Yes

Classify in appropriate category

No

Does the mixture contain one or more ingredients classified as a Category 1 target organ systemic toxicant at a concentration of:
• ≥ 1.0% ?
• ≥ 10% ?
See Table 2 of this Chapter for explanation of cut-off values/concentration limits.

Yes

Category 1
New Symbol
Danger

No

Does the mixture contain one or more ingredients classified as a Category 1 target organ systemic toxicant at a concentration of:
• ≥ 1.0 and < 10% ?
See Table 2 of this Chapter for explanation of cut-off values/concentration limits.

Yes

Category 2
New Symbol
Warning

No

Does the mixture contain one or more ingredients classified as a Category 2 target organ systemic toxicant at a concentration of:
• ≥ 1.0%?
• ≥ 10% ?
See Table 2 of this Chapter for explanation of cut-off values/concentration limit.

Yes

Category 2
New Symbol
Warning

No

Not classified

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4 See paragraphs 7-25 of this Chapter and “The Use of Cut-off Values/Concentration Limits” in Chapter 1.2.
5 See paragraphs 35-38 and Table 2 for explanation and guidance.

Replace the Decision Logic for classification of Target Organ Systemic Toxicity, repeated exposure, by the following:

**Decision Logic for Classification of Target Organ Systemic Toxicity following Repeated Exposure**

The decision logic, which follows, is not part of the harmonised classification system, but has been provided here as additional guidance only. The responsible person for classification is strongly recommended to study the criteria before and during use of the decision logic.

**Substance:** Does the substance have data and/or information to evaluate target organ systemic toxicity following repeated exposure?

- Yes → Classification not possible
- No → See Decision logic 2

**Mixture:** Does the mixture as a whole or its ingredients have data/information to evaluate target organ systemic toxicity following repeated exposure?

- Yes → Classification not possible
- No → See Decision logic 2

**Following repeated exposure**
- Can the substance or mixture produce significant toxicity in humans, or
- can it be presumed to have the potential to produce significant toxicity in humans on the basis of evidence from studies in experimental animals?

See paragraphs 7-29 for criteria and guidance including values. Application of the criteria needs expert judgment in a weight of evidence approach.

- Yes → Category 1
- No → Not classified

**Following repeated exposure,**
- can the substance or mixture be presumed, to have the potential on the basis of evidence from studies in experimental animals, to be harmful to human health?

See paragraphs 7-29 for criteria and guidance including values. Application of the criteria needs expert judgment in a weight of evidence approach.

- Yes → Category 2
- No → Not classified

Continued on next page
In this chapter, see paragraphs 7-29, Tables 1 and 2, and in Chapter 1.2, see “The Use of Cut-off Values/Concentration Limits”.

See paragraphs 39-43 and Table 3 for explanation and guidance.
Replace the Decision Logic and Guidance on page 79 by the following:

**Decision Logic for Classification of Hazardous to the Aquatic Environment**

The decision logic, which follows, is not part of the harmonised classification system, but has been provided here as additional guidance only. The responsible person for classification is strongly recommended to study the criteria before and during use of the decision logic.

**Substance:** Is there sufficient information (toxicity, degradation, bioaccumulation) for classification?

- **No** Classification not possible
- **Yes**

**Acute**

Does it have an:
- 96 hr LC$_{50}$ (fish) $\leq$ 1 mg/L, and/or
- 48 hr EC$_{50}$ (crustacea) $\leq$ 1 mg/L, and/or
- 72 or 96 hr ErC$_{50}$ (algae or other aquatic plants) $\leq$ 1 mg/L?

- **Yes** Acute Category 1 Warning
- **No**

**Chronic**

- Does it lack the potential to rapidly degrade? and/or
- Does it have the potential to bioaccumulate (BCF $\geq$ 500 or if absent, log Kow $\geq$ 4)? See Note 4 of Table 1 and Chapter 5 of Annex 9.

- **No**
- **Yes** Chronic Category 1 Warning

**Acute**

Does it have an:
- 96 hr LC$_{50}$ (fish) $\leq$ 10 mg/L, and/or
- 48 hr EC$_{50}$ (crustacea) $\leq$ 10 mg/L, and/or
- 72 or 96 hr ErC$_{50}$ (algae or other aquatic plants) $\leq$ 10 mg/L?

- **Yes** Acute Category 2
- **No**

**Chronic**

- Does it lack the potential to rapidly degrade? and/or
- Does it have the potential to bioaccumulate (BCF $\geq$ 500 or if absent, log Kow $\geq$ 4)? See Note 4 of Table 1 and Chapter 5 of Annex 9.

- **No**
- **Yes** Chronic Category 2

Continued on next page
Labelling requirements differ from one regulatory system to another, and certain classification categories may only be used in one or a few regulations.

See Table 1, Note 5 further developed in Annex 9, paragraphs 66 and 67.
Mixture: Does the mixture as a whole have aquatic toxicity data for fish, crustacea, and algae/aquatic plants?

Yes

Values from Mixture Decision Logic 2

Acute
Does it have a 96 hr LC_{50} (fish), 48 hr EC_{50} (crustacea), or 72 or 96 hr ErC_{50} (algae or other aquatic plants)
• \(\leq 1\) mg/L?

No

Acute Category 1
Warning

Acute
Does it have a 96 hr LC_{50} (fish), 48 hr EC_{50} (crustacea), or 72 or 96 hr ErC_{50} (algae or other aquatic plants)
• \(\leq 10\) mg/L?

Yes

Acute Category 2

No

Acute
Does it have a 96 hr LC_{50} (fish), 48 hr EC_{50} (crustacea), or 72 or 96 hr ErC_{50} (algae or other aquatic plants)
• \(\leq 100\) mg/L?

Yes

Acute Category 3

No

Not classified for acute

Chronic
See Decision Logic 3 for Chronic Classification

Continued on next page

5 Labelling requirements differ from one regulatory system to another, and certain classification categories may only be used in one or a few regulations.
Labelling requirements differ from one regulatory system to another, and certain classification categories may only be used in one or a few regulations.

If not all components have information, include the statement "x percent of the mixture consists of ingredients(s) of unknown hazards to the aquatic environment" on the label. Alternatively, in the case of a mixture with highly toxic ingredients, if toxicity values are available for these highly toxic ingredients and all other ingredients do not significantly contribute to the hazard of the mixture, than the additivity formula may be applied. (See paragraph 56). In this case and other cases where toxicity values are available for all ingredients, the acute classification may be made solely on the basis of the additivity formula.

For explanation of M factor see paragraph 56.
Mixtures decision logic 2 (Additivity method)

Apply the Additivity Method:
\[
\frac{\sum Ci}{L(E)C_{50 m}} = \sum \frac{Ci}{L(E)C_{50}}
\]

where:
- \( C_i \) = concentration of component \( i \) (weight percentage)
- \( L(E)C_{50i} \) = (mg/L) LC50 or EC50 for component \( i \)
- \( \eta \) = number of components
- \( L(E)C_{50 m} \) = \( L(E)C_{50} \) of the part of the mixture

Mixtures decision logic 3 (Chronic classification)

Sum of ingredients classified as:
- Chronic 1 \( \times \) M^{0.5} \( \geq \) 25%?
  - Yes
  - Chronic Category 1
  - Warning

No

Sum of ingredients classified as:
- (Chronic 1 \( \times \) M^{0.1} \( \times \) 10) + Chronic 2 \( \geq \) 25%?
  - Yes
  - Chronic Category 2

No

Sum of ingredients classified as:
- (Chronic 1 \( \times \) M^{0.1} \( \times \) 100) + (Chronic 2 \( \times \) 10) + Chronic 3 \( \geq \) 25%?
  - Yes
  - Chronic Category 3

No

Sum of ingredients classified as:
- Chronic 1 + Chronic 2 + Chronic 3 + Chronic 4 \( \geq \) 25%?
  - Yes
  - Chronic Category 4
EXAMPLES

Under Review

No

Not classified chronic