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**COMMITTEE OF EXPERTS ON THE TRANSPORT OF
DANGEROUS GOODS AND ON THE GLOBALLY
HARMONIZED SYSTEM OF CLASSIFICATION
AND LABELLING OF CHEMICALS**

Sub-Committee of Experts on the Globally Harmonized System
of Classification and Labelling of Chemicals

Seventh session, 14-16 July 2004
Item 2 (b) (iv) of the provisional agenda

**UPDATING OF THE GLOBALLY HARMONIZED SYSTEM OF CLASSIFICATION AND
LABELLING OF CHEMICALS (GHS)**

Health hazards

Proposal for revision of Chapter 3.8:

Inclusion of Classification Criteria for Respiratory Tract Irritation and Narcotic Effects

Transmitted by the Organization for Economic Co-operation and Development (OECD)

1. In December 2002, the UN Sub-Committee of Experts on the GHS requested that the OECD completes the ongoing work on classification criteria for Respiratory Tract Irritation (RTI) and Narcotic Effects.
2. The OECD considered several options regarding how to integrate RTI and Narcotic Effects Classification Criteria into the GHS and agreed to include them in Chapter 3.8 as Category 3. However, **this agreement was under the condition that differences amongst Category 1, Category 2 and Category 3 are clearly stressed in the chapter and that cross-references ensure visibility regarding what is included in Chapter 3.8.**
3. The main changes in the proposed revised Chapter 3.8 are:
 - the addition of Category 3 (Figure 3.8.1);
 - the specification of the criteria for RTI and for Narcotic Effects (Paragraph 3.8.3);
 - the inclusion of a paragraph for mixtures which contain Category 3 ingredients (Paragraph 3.8.4.4.5); and
 - the inclusion of a Signal Word, a Hazard Statement and an optional Symbol for Category 3 (Table 3.8.3).

4. The other proposed changes are exclusively for a clear distinction of Category 3 from the two other categories, for visibility and for consistency.

5. Other changes, which do not refer directly to the mandate given by the UN Sub-Committee, would facilitate the implementation of Chapter 3.8; these changes may be proposed at a later stage.

Proposal

3.8.1.1 Insert “and not specifically addressed in chapters 3.1 to 3.7” between “delayed” and “are included”.

At the end of the paragraph, insert “See also Paragraph 3.8.1.6”.

3.8.1.6 Replace the last sentence with the following:

“Other specific toxic effects, listed below are assessed separately in the GHS and consequently are not included here:

- acute lethality/toxicity (Chapter 3.1),
- skin corrosivity/irritation (Chapter 3.2),
- serious damage to eyes/irritation (Chapter 3.3),
- skin and respiratory sensitization (Chapter 3.4),
- mutagenicity (Chapter 3.5),
- carcinogenicity (Chapter 3.6), and
- reproductive toxicity (Chapter 3.7).”

After Paragraph 3.8.1.6, insert a new Paragraph 3.8.1.7 as follows:

“3.8.1.7 The classification criteria in this chapter are organized as criteria for substances Categories 1 and 2 (3.8.2), criteria for substances Category 3 (3.8.3) and criteria for mixtures (3.8.4). See Figure 3.8.1.”

3.8.2 In the title, insert “-Category 1 and 2” after “Classification criteria for substances”;

3.8.2.1 Replace “one of two categories” with “Category 1 or Category 2”.

At the end of this paragraph, insert “(Figure 3.8.1)”.

Figure 3.8.1 Insert above “**NOTE**” at the bottom of the box the following text:

“CATEGORY 3: Transient Target Organ effects

There are target organ effects for which a substance/mixture may not meet the criteria to be classified in Categories 1 or 2 indicated above. These are effects which adversely alter human function for a short duration after exposure and from which humans may recover in a reasonable period without leaving significant alteration of structure or function. This category only includes narcotic effects and respiratory tract irritation. Substances/mixture may be classified specifically for these effects as discussed in 3.8.3.”

In the first line of the note, replace “both” with “these”.

3.8.2.7 In the title, insert “for Category 1 and 2” after “Effects considered to support classification”.

3.8.2.7.3 In the first line of the second bullet, replace “in the” with “, more than transient in nature, in the respiratory system,”;

In the second bullet, insert “,other organs” between “peripheral nervous systems” and “or other organ systems”.

3.8.2.8 In the title, insert “for Category 1 and 2” after “Effects considered not to support classification”;

Delete the sixth bullet.

3.8.2.9 In the title, insert “for Category 1 and 2” after “experimental animals”.

Table 3.8.1 Insert “¹” at the end of the title of the table and text for category 3 in the box as follows:

Table 3.8.1: Guidance value ranges for single-dose exposures¹

		Guidance value ranges for :		
Route of exposure	Units	Category 1	Category 2	Category 3
Oral (rat)	mg/kg body weight	$C \leq 300$	$2000 \geq C > 300$	Guidance values do not apply ²
Dermal (rat or rabbit)	mg/kg body weight	$C \leq 1000$	$2000 \geq C > 1000$	
Inhalation (rat) gas	Ppm	$C \leq 2500$	$5000 \geq C > 2500$	
Inhalation (rat) vapour	mg/l	$C \leq 10$	$20 \geq C > 10$	
Inhalation (rat) dust/mist/ Fume	mg/l/4h	$C \leq 1.0$	$5.0 \geq C > 1.0$	

Insert “**NOTE 1**” before the note under the table;

Insert a new note after “**NOTE 1**” as follows:

NOTE 2: *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.*

3.8.3 Replace with a new section **3.8.3** as follows:

“3.8.3 Classification criteria for substances -- Category 3

3.8.3.1 Criteria for Respiratory Tract Irritation

The criteria for respiratory tract irritation as category 3 are:

- Respiratory irritant effects (characterized by localised redness, edema, pruritis and/or pain) that impair function with symptoms such as cough, pain, choking, and breathing difficulties are included. It is recognized that this evaluation is based primarily on human data.
- Subjective human observations could be supported by objective measurements of clear respiratory tract irritation (RTI) (eg. electrophysiological responses, biomarkers of inflammation in nasal or bronchoalveolar lavage fluids).
- The symptoms observed in humans should also be typical of those that would be produced in the exposed population rather than being an isolated idiosyncratic reaction or response triggered only in individuals with hypersensitive airways. Ambiguous reports simply of 'irritation' should be excluded as this term is commonly used to describe a wide range of sensations including those such as smell, unpleasant taste, a tickling sensation, and dryness, which are outside the scope of this classification endpoint.
- 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.
- This special classification would occur only when more severe organ/systemic effects including in the respiratory system are not observed.

3.8.3.2 *Criteria for Narcotic effects*

The criteria for Narcotic Effects as category 3 are:

- Central nervous system depression including narcotic effects in humans such as drowsiness, narcosis, reduced alertness, loss of reflexes, lack of coordination, and vertigo are included. These effects can also be manifested as severe headache or nausea, and can lead to reduced judgment, dizziness, irritability, fatigue, impaired memory function, deficits in perception and coordination, reaction time, or sleepiness.
- Narcotic effects observed in animal studies may include lethargy, lack of coordination righting reflex, narcosis, and ataxia. If these effects are not transient in nature, than they should be considered for classification as category 1 or 2.”;

3.8.4 Replace with original section 3.8.3 and renumber accordingly;

Insert a new paragraph 3.8.4.4.5 after the renumbered paragraph 3.8.4.4.4 as follows:

“3.8.4.4.5 Care should be exercised when extrapolating toxicity of a mixture that contains category 3 ingredient(s). A cut off value of 20% has been suggested; however, it should be

recognised that this cut-off value may be higher or less depending on the Category 3 ingredient(s) and that some effects such as respiratory tract irritation may not occur below a certain concentration while other effects such as narcotic effects may occur below this 20% value. Expert judgment should be exercised.”

3.8.5 Replace with original section **3.8.4** and renumber accordingly.

Table 3.8.2 Insert “as category 1 or 2” at the end of the table title

Table 3.8.3 Insert text for category 3 in the box as follows:

	Category 1	Category 2	Category 3
Symbol	Health Hazard	Health Hazard	Exclamation Mark (optional)
Signal word	Danger	Warning	Warning
Hazard statement	Causes damage to organs (or state all organs affected, if known) if (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)	May cause damage to organs (or state all organs affected, if known) if (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)	May cause respiratory irritation or May cause drowsiness and dizziness

Renumber original section **3.8.5** as **3.8.6**.

In the Decision logic 3.8.1, insert in the appropriate format, before the last arrow on the left and the last box on the right, the following:

No




Following single exposure, <ul style="list-style-type: none"> Can the substance or the mixture produce Narcotic Effects or Respiratory Tract Irritation? See 3.8.3 for criteria. Application of the criteria needs expert judgment in a weigh of evidence approach. 	Yes 	Category 3 (Optional) Warning
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In the Decision logic 3.8.2, insert in the appropriate format, before the last arrow on the left and the last box on the right, the following:

No



<p>Does the mixture contain one or more ingredients classified as Category 3 target organ systemic toxicant at a concentration > 20%? See 3.8.4.4.5 Care should be exercised when classifying such mixtures.</p>	<p>Yes →</p>	<p>Category 3  (Optional) Warning</p>
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