

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 3 of the provisional agenda

Classification criteria and related hazard communication

Update on the work of the informal correspondence group on practical classification issues

Transmitted by the expert from the United States of America on behalf of the informal correspondence group on Practical Classification Issues

A. Purpose

1. The purpose of this document is to provide an update on the work undertaken by the informal correspondence group on Practical Classification Issues (PCI).

B. Background

2. At its 28th session, the Sub-Committee approved the program of work to be undertaken by the practical classification issues informal correspondence group for the current biennium (UN/SCEGHS/28/INF.32).
3. The PCI met during the 28th and 29th sessions for discussion of several proposals to modify the GHS text outlined in the agreed program of work. Based on discussions during these meetings, the PCI has reached agreement for the proposed editorial amendments to the GHS text for items (a), (d) and (g) from the program of work as presented in the Annex to this document.

C. Next steps

4. Pending feedback from this document, the PCI group plans to submit a working paper for the 31st session for consideration by the Subcommittee.

Annex 1

Proposed editorial amendments to the GHS text

Item (a):

Review the definitions in each of the health hazard chapters for consistency in the way the definitions are provided. For example, some definitions are taken directly from OECD test guidelines while others are more general (i.e., they don't refer to specific tests).

Background: In order to progress this item, the working group agreed to apply the following set of guiding principles as each definition was reviewed:

- Definitions should be:
 - General and neutral with respect to test guidelines and not include test guideline criteria as part of a definition.
 - Clear and concise.
 - Provide a clear differentiation between the “definition” and the “general considerations” text when present in a chapter.
 - Make use as far as possible the existing text in the GHS.
 - Consistently note that the definition applies to a “substance or mixture” and avoid using the term “chemical”.

Proposed definitions:

Chapter 3.1 Acute toxicity

Draft working definition:

Acute toxicity refers to serious adverse health effects (e.g., lethality) occurring after a single or short-term oral, dermal or inhalation exposure to a substance or mixture.

Original definition:

Acute toxicity refers to those adverse effects occurring following oral or dermal administration of a single dose of a substance, or multiple doses given within 24 hours, or an inhalation exposure of 4 hours.

Chapter 3.2 Skin corrosion/irritation

Draft working definitions:

Skin corrosion is the production of irreversible damage to the skin; namely, visible necrosis through the epidermis and into the dermis occurring after exposure to a substance or mixture.

Skin irritation is the production of reversible damage to the skin occurring after exposure to a substance or mixture.

Original definitions:

Skin corrosion is the production of irreversible damage to the skin; namely, visible necrosis through the epidermis and into the dermis, following the application of a test substance for up to 4 hours. Corrosive reactions are typified by ulcers, bleeding, bloody scabs, and, by the end of observation at 14 days, by discolouration due to blanching of the skin, complete areas of alopecia, and scars. Histopathology should be considered to evaluate questionable lesions.

Skin irritation is the production of reversible damage to the skin following the application of a test substance for up to 4 hours.

Chapter 3.3 serious eye damage /eye irritation

Draft working definitions:

Serious eye damage is the production of tissue damage in the eye, or serious physical decay of vision, which is not fully reversible, occurring after exposure of the eye, to a substance or mixture.

Eye irritation is the production of changes in the eye, which are fully reversible, occurring after exposure of the eye, to a substance or mixture.

Original definitions:

Serious eye damage is the production of tissue damage in the eye, or serious physical decay of vision, following application of a test substance to the anterior surface of the eye, which is not fully reversible within 21 days of application.

Eye irritation is the production of changes in the eye following the application of test substance to the anterior surface of the eye, which are fully reversible within 21 days of application.

Chapter 3.4 Respiratory or skin sensitization

Draft working definitions:

Respiratory sensitization refers to hypersensitivity of the airways after inhalation of a substance or a mixture.

Skin sensitization refers to an allergic response after skin contact with a substance or a mixture.

Original definition:

A *respiratory sensitizer* is a substance that will lead to hypersensitivity of the airways following inhalation of the substance.

A *skin sensitizer* is a substance that will lead to an allergic response following skin contact.

Chapter 3.5 Germ cell mutagenicity

3.5.1 Definitions and general considerations

3.5.1.1 *Germ cell mutagenicity refers to heritable gene mutations, and heritable structural and numerical chromosome aberrations in germ cells occurring after exposure to a substance or mixture.*

3.5.1.2 This hazard class is primarily concerned with chemicals that may cause mutations in the germ cells of humans that can be transmitted to the progeny. However, mutagenicity/genotoxicity tests *in vitro* and in mammalian somatic cells *in vivo* are also considered in classifying substances and mixtures within this hazard class.

3.5.1.23 In the present context, commonly found definitions of the terms “mutagenic”, “mutagen”, “mutations” and “genotoxic” are used. A *mutation* is defined as a permanent change in the amount or structure of the genetic material in a cell.

3.5.1.34 The term *mutation* applies both to heritable genetic changes that may be manifested at the phenotypic level and to the underlying DNA modifications when known (including, for example, specific base pair changes and chromosomal translocations). The term *mutagenic* and *mutagen* will be used for agents giving rise to an increased occurrence of mutations in populations of cells and/or organisms.

3.5.1.45 The more general terms *genotoxic* and *genotoxicity* apply to agents or processes which alter the structure, information content, or segregation of DNA, including those which cause DNA damage by interfering with normal replication processes, or which in a non-physiological manner (temporarily) alter its replication. Genotoxicity test results are usually taken as indicators for mutagenic effects.

Chapter 3.6 carcinogenicity

3.6.1 Definitions

Carcinogenicity refers to the induction of cancer or an increase in the incidence of cancer after exposure to a substance or mixture. The term carcinogen denotes a substance or a mixture which induces cancer or increases its incidence. Substances and mixtures which have induced benign and malignant tumours in well performed experimental studies on

animals are considered also to be presumed or suspected human carcinogens unless there is strong evidence that the mechanism of tumour formation is not relevant for humans.

Classification of a substance or mixture as posing a carcinogenic hazard is based on its inherent properties and does not provide information on the level of the human cancer risk which the use of the substance or mixture may represent.

Chapter 3.7 Reproductive toxicity

3.7.1 Definitions and general considerations

3.7.1.1 *Reproductive toxicity*

Reproductive toxicity ~~includes~~ refers to adverse effects on sexual function and fertility in adult males and females, as well as developmental toxicity in the offspring, occurring after exposure to a substance or mixture. The definitions presented below are adapted from those agreed as working definitions in IPCS/EHC Document N°225 *Principles for evaluating health risks to reproduction associated with exposure to chemicals*. For classification purposes, the known induction of genetically based inheritable effects in the offspring is addressed in *Germ cell mutagenicity* (Chapter 3.5), since in the present classification system it is considered more appropriate to address such effects under the separate hazard class of germ cell mutagenicity.

In this classification system, reproductive toxicity is subdivided under two main headings:

- (a) Adverse effects on sexual function and fertility;
- (b) Adverse effects on development of the offspring.

Some reproductive toxic effects cannot be clearly assigned to either impairment of sexual function and fertility or to developmental toxicity. Nonetheless, ~~chemicals~~ substances and mixtures with these effects would be classified as reproductive toxicants with a general hazard statement.

Chapter 3.8 Specific target organ toxicity single exposure

3.8.1 Definitions and general considerations

3.8.1.1 The purpose of this chapter is to provide a means of classifying substances and mixtures that produce specific, non lethal target organ toxicity arising from a single exposure. All significant health effects that can impair

function, both reversible and irreversible, immediate and/or delayed and not specifically addressed in chapters 3.1 to 3.7 and 3.10 are included (see also para. 3.8.1.6).

Proposed 3.8.1.1: *Specific target organ toxicity – single exposure* refers to specific, non-lethal toxic effects on target organs that arise from a single exposure to a substance or mixture. All significant health effects that can impair function, both reversible and irreversible, immediate and/or delayed and not specifically addressed in chapters 3.1 to 3.7 and 3.10 are included (see also para. 3.8.1.6).

[Note: there is currently no definition for Specific Target Organ Toxicity-Single Exposure in Chapter 3.8 of the GHS. Therefore, there is no existing definition for a comparison]

Chapter 3.9 Specific target organ toxicity repeated exposure

3.9.1 Definitions and general considerations

3.9.1.1 The purpose of this chapter is to provide a means of classifying substances and mixtures that produce specific target organ toxicity arising from a repeated exposure. All significant health effects that can impair function, both reversible and irreversible, immediate and/or delayed are included.

Proposed 3.9.1.1: *Specific target organ toxicity – repeated exposure* refers to specific toxic effects on target organs that arise from repeated exposure to a substance or mixture. All significant health effects that can impair function, both reversible and irreversible, immediate and/or delayed are included.

[Note: there is currently no definition for Specific Target Organ Toxicity-Repeated Exposure in Chapter 3.9 of the GHS. Therefore, there is no existing definition for a comparison]

Chapter 3.10 Aspiration hazard

3.10.1 Definitions and general and specific considerations

~~3.10.1.1 The purpose of this chapter is to provide a means of classifying substances or mixtures that may pose an aspiration toxicity hazard to humans.~~

3.10.1.34 *Aspiration toxicity hazard* ~~includes~~ refers to severe acute effects such as chemical pneumonia, varying degrees of pulmonary injury or death ~~following~~ after aspiration of a substance or mixture.

3.10.1.2 *Aspiration* means the entry of a liquid or solid chemical directly through the oral or nasal cavity, or indirectly from vomiting, into the trachea and lower respiratory system.

3.10.1.4 Aspiration is initiated at the moment of inspiration, in the time required to take one breath, as the causative material lodges at the crossroad of the upper respiratory and digestive tracts in the laryngopharyngeal region.

3.10.1.5 Aspiration of a substance or mixture can occur as it is vomited following ingestion. This may have consequences for labelling, particularly where, due to acute toxicity, a recommendation may be considered to induce vomiting after ingestion. However, if the substance/mixture also presents an aspiration toxicity hazard, the recommendation to induce vomiting may need to be modified.

Item (d):

Propose an editorial revision to the last sentence in GHS paragraph 3.1.2.3, which provides guidance on the use of data when evaluating acute toxicity “in several animal species”. Currently, reference to effect in humans is only contained in a footnote (g) to Table 3.1.1 and with many competent authorities not selecting Category 5 the human reference has been lost in implementing regulations. The goal of the proposed editorial revision is to make clear that both data from animal tests and human epidemiological studies should be considered.

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 judgment should be used in selecting the most appropriate LD₅₀ value from among valid, well-performed tests. In cases where data from human experience (i.e., occupational data, data from accident databases, epidemiology studies) is also available, it should be considered in a weight of evidence approach consistent with the principles described in section 1.3.2.4.9 *Weight of evidence*.

Item (g):

Propose updating Table 3.1.1 to express acute toxicity values as a range. For example, acute toxicity values for acute oral toxicity Category 3 would be expressed as > 50 and ≤ 300 or 50 < ATE ≤ 300.

Replace Table 3.1.1 with the following:

**~~Table 3.1.1: Acute toxicity hazard categories and acute toxicity estimate (ATE) values~~
defining the respective categories Acute toxicity estimate (ATE) values and criteria for acute toxicity hazard categories**

Exposure route	Category 1	Category 2	Category 3	Category 4	Category 5
Oral (mg/kg bodyweight) <i>See notes (a) and (b)</i>	ATE ≤ 5	5 < ATE ≤ 50	50 < ATE ≤ 300	300 < ATE ≤ 2000	5000 <i>See detailed criteria in Note (g)</i>
Dermal (mg/kg bodyweight) <i>See notes (a) and (b)</i>	ATE ≤ 50	50 < ATE ≤ 200	200 < ATE ≤ 1000	1000 < ATE ≤ 2000	
Gases (ppmV) <i>See notes (a), (b) and (c)</i>	ATE ≤ 100	100 < ATE ≤ 500	500 < ATE ≤ 2500	2500 < ATE ≤ 20000	<i>See detailed criteria in Note (g)</i>
Vapours (mg/l) <i>See notes (a), (b), (c), (d) and (e)</i>	ATE ≤ 0.5	0.5 < ATE ≤ 2.0	2.0 < ATE ≤ 10.0	10.0 < ATE ≤ 20.0	
Dusts and Mists (mg/l) <i>See notes (a), (b), (c) and (f)</i>	ATE ≤ 0.05	0.05 < ATE ≤ 0.5	0.5 < ATE ≤ 1.0	1.0 < ATE ≤ 5.0	

Note: Gases concentration are expressed in parts per million per volume (ppmV).