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,
agenda item 2, b, i)

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

Proposal for revision of Chapter 3.1: rationale

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

In December 2002, the UN Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals requested that OECD, during the biennium 2003-2004, among other things:

- completes the on-going work on classification criteria for substances, which in contact with water release toxic/corrosive gases and for respiratory tract irritation;

- revises the classification criteria for acute toxicity to take account of the experimentally obtained acute toxicity range estimates to point estimates for the respective routes of exposure;

- defines the terms for dust, mist and vapour in relation to inhalation toxicity.

The attached proposal for revision of Chapter 3.1 includes:

(i) optional additional labelling of substances and mixtures for which data are available that indicates that the mechanism of toxicity was corrosion of the respiratory tract when inhaled: see new Paragraph 3.1.2.6.5 and Note I to Table 3.1.3;

(ii) several slight changes in paragraph 3.1.2.1, in Tables 3.1.1 and 3.1.2 to clarify that the existing conversion rate that may have been perceived as only applicable to mixtures also applies to substances;

(iii) definitions of “dust”, “mist” and “vapour” with general information on formation processes and size range in Note (d) under Table 3.1.1.

The proposed definitions are short and simple; information on formation processes and size is not included in the definition since agreement on details would take considerable time and is not needed in this context:

Paragraph 3.1.2.6.4 was missing in GHS Chapter 3.1, but later inserted in (Corrigendum UN/SCEGHS/5/INF.7).

PROPOSAL FOR REVISION OF CHAPTER 3.1

3.1.2.1 Insert in the second line "cut-off" between "numeric" and "criteria"; insert "as shown inthe table below. Acute toxicity values are" between "criteria" and "expressed". In the third line, insert "or as acute toxicity estimates (ATE)" after "LC50 (inhalation) values" In the third line, delete "as shown in the table below".

Table 3.1.1 Insert a new Note (a) under Table 3.1.1 as follows:

"*a) the acute toxicity estimate (ATE) for the classification of a substance or ingredient in a mixture is derived using:*
- *the DL50/LC50 where available,*
- *the appropriate conversion value from Table 3.1.2 that relates to the results of a range test or*
- *the appropriate conversion value from Table 3.1.2 that relates to a classification category*"

Rename accordingly Notes (a) to (e): "Notes (b) to (f)"

In the renamed Note (d), replace the last sentence with the following:

"*The terms "dust", "mist" and "vapour" are defined as follows:*

⇊ *dust : solid particles of a substance or mixture suspended in a gas (usually air) mist: liquid droplets of a substance or mixture suspended in a gas (usually air) vapour: the gaseous form of a substance or mixture released from its liquid or solid state.*

Dust is generally formed by mechanical processes. Mist is generally formed by condensation of supersatured vapours or by physical shearing of liquids. Dusts and mists generally have sizes ranging from less than 1 to about 100 µm ".

In the left column of Table 3.1.1, insert "Note (a)" in cells for Oral and Dermal Exposures, "Note (b)" in the cells for Gases and for Dusts and Mists, "Note (d)" in the box for Vapours and "Note (e)" in the box for Dusts and Mists. Delete "Note (d)" in the box for Dust and Mists.

In the right column of Table 3.1.1, replace "Note (e)" with "Note (f)".

3.1.2.5 In the footnote on page 111, replace "Note (e)" with "Note (f)"

3.1.2.6.4 After paragraph 3.1.2.6.4, insert Paragraph 3.1.2.6.5 as follows:

"3.1.2.6.5 In addition to classification for inhalation toxicity, if data are available that indicates that the mechanism of toxicity was corrosivity of the substance or mixture, certain authorities may also label it as *corrosive to the respiratory tract.* Corrosion of the respiratory tract is defined by destruction of the respiratory tract tissue after a single, limited period of exposure analogous to skin corrosion; this includes destruction of the mucosa. The corrosivity evaluation could be based on expert judgment using such evidence as: human and animal experience, existing (*in vitro)* data, pH values, information from similar substances or any other pertinent data."

Table 3.1.2 In the title of the table, insert "for classification" between "toxicity point estimates" and "for the respective routes";

In the Note 2, under the table, insert in the first line “classification of” between “ATE for” and “a mixture”.

Table 3.1.3 In the first column, bottom left cell of the table, insert “Note 1” after “Inhalation”

Under Table 3.1.3, insert the following note:

“Note 1: If a substance/mixture is also determined to be corrosive (based on data such as skin or eye data), corrosivity hazard may also be communicated by some authorities as symbol and/or hazard statement. That is, in addition to an appropriate acute toxicity symbol, a corrosivity symbol (used for skin and eye corrosivity) may be added along with a corrosivity hazard statement such as “corrosive” or “corrosive to the respiratory tract”.

3.1.3.3 Delete (b); rename accordingly “(c)”: “(b)”

Annex

**PROPOSAL FOR REVISION OF
GHS CHAPTER 3.1: ACUTE TOXICITY**

3.1.1 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.

3.1.2 Classification criteria for substances

3.1.2.1 Chemicals can be allocated to one of five toxicity categories based on acute toxicity by the oral, dermal or inhalation route according to the numeric cut-off criteria as shown in the table below. Acute toxicity values are expressed as (approximate) LD50 (oral, dermal) or LC50 (inhalation) values or as acute toxicity estimates (ATE) ~~as shown in the table below.~~ Explanatory notes are shown following the table.

Table 3.1.1: Acute toxicity hazard categories and (approximate) LD50/LC50 values defining the respective categories

Exposure Route	Category 1	Category 2	Category 3	Category 4	Category 5
Oral (mg/kg bodyweight) *see: Note (a)*	?5	?50	?300	?2000	?5000
Dermal (mg/kg bodyweight) *see: Note (a)*	?50	?200	?1000	?2000	
Gases (ppmV) *see: Note (a)* *Note (b)*	?100	?500	?2500	?5000	*See detailed criteria in Note (~~e~~f)*
Vapours (mg/l) *see: Note (a)* *Note (b)* *Note (c)* *Note (d)*	?0.5	?2.0	?10	?20	
Dusts and Mists (mg/l) *see: Note (a)* *Note (~~d~~b)* *Note (e)*	?0.05	?0.5	?1.0	?5	

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

Notes to Table 3.1.1:

(a) The acute toxicity estimate (ATE) for the classification of a substance or ingredient in a mixture is derived using:

- The LD_{50}/LC_{50} where available,
- The appropriate conversion value from Table 3.1.2 that relates to the results of a range test or
- The appropriate conversion value from Table 3.1.2 that relates to a classification category;

(b ~~a~~) *Inhalation cut-off values in the table are based on 4 hour testing exposures. Conversion of existing inhalation toxicity data which has been generated according to 1 hour exposures should be by dividing by a factor of 2 for gases and vapours and 4 for dusts and mists;*

(c ~~b~~) It is recognised that saturated vapour concentration may be used as an additional element by some regulatory systems to provide for specific health and safety protection. (e.g. UN Recommendations for the Transport of Dangerous Goods);

(d ~~(c)~~) For some chemicals the test atmosphere will not just be a vapour but will consist of a mixture of liquid and vapour phases. For other chemicals the test atmosphere may consist of a vapour which is near the gaseous phase. In these latter cases, classification should be based on ppmV as follows: Category 1 (100 ppmV), Category 2 (500 ppmV), Category 3 (2500 ppmV), Category 4 (5000 ppmV). ~~Work in the OECD Test Guidelines Programme should be undertaken to better define t~~The terms "dust~~s~~", "mist~~s~~" and "vapour~~s~~" ~~in relation to inhalation toxicity testing~~ are defined as follows:

- *dust: solid particles of a substance or mixture suspended in a gas (usually air)*
- *mist: liquid droplets of a substance or mixture suspended in a gas (usually air)*
- *vapour: the gaseous form of a substance or mixture released from its liquid or solid state*

Dust is generally formed by mechanical processes. Mist is generally formed by condensation of supersatured vapours or by physical shearing of liquids. Dust and mists generally have sizes ranging from less than 1 to about 100 µm.

(d ~~e~~) The values for dusts and mists should be reviewed to adapt to any future changes to OECD Test Guidelines with respect to technical limitation in generating, maintaining and measuring dust and mist concentrations in respirable form;

(f ~~e~~) Criteria for Category 5 are intended to enable the identification of substances which are of relatively low acute toxicity hazard but which under certain circumstances may present a danger to vulnerable populations. These substances are anticipated to have an oral or dermal LD_{50} in the range of 2000-5000 mg/kg bodyweight and equivalent doses for inhalation. The specific criteria for Category 5 are:

(*i*) *The substance is classified in this Category if reliable evidence is already available that indicates the LD_{50} (or LC_{50}) to be in the range of Category 5 values or other animal studies or toxic effects in humans indicate a concern for human health of an acute nature.*

(ii) The substance is classified in this Category, through extrapolation, estimation or measurement of data, if assignment to a more hazardous category is not warranted, and:

- *reliable information is available indicating significant toxic effects in humans; or*
- *any mortality is observed when tested up to Category 4 values by the oral, inhalation, or dermal routes; or*
- *where expert judgement confirms significant clinical signs of toxicity, when tested up to Category 4 values, except for diarrhoea, piloerection or an ungroomed appearance; or*
- *where expert judgement confirms reliable information indicating the potential for significant acute effects from other animal studies.*

Recognising the need to protect animal welfare, testing in animals in Category 5 ranges is discouraged and should only be considered when there is a strong likelihood that results of such a test would have a direct relevance for protecting human health.

3.1.2.2 The harmonized classification system for *acute toxicity* has been developed in such a way as to accommodate the needs of existing systems. A basic principle set by the IOMC Coordinating Group/Harmonization of Chemical Classification Systems (CG/HCCS) is that "harmonization means establishing a common and coherent basis for chemical hazard classification and communication from which the appropriate elements relevant to means of transport, consumer, worker and environment protection can be selected". To that end, five categories have been included in the acute toxicity scheme.

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_{50} value from among valid, well-performed tests.

3.1.2.4 Category 1, the highest toxicity category, has cut-off values (see Table 3.1.1) currently used primarily by the transport sector for classification for packing groups.

3.1.2.5 Category 5 is for chemicals which are of relatively low acute toxicity but which, under certain circumstances, may pose a hazard to vulnerable populations. Criteria for identifying substances in Category 5 are provided in addition to the table. These substances are anticipated to have an oral or dermal LD_{50} value in the range 2000 - 5000 mg/kg bodyweight and equivalent doses for inhalation exposure[1]. In light of animal welfare considerations, testing in animals in Category 5 ranges is discouraged and should only be considered when there is a strong likelihood that results of such testing would have a direct relevance to the protection of human health.

3.1.2.6 *Specific considerations for inhalation toxicity*

3.1.2.6.1 Values for *inhalation toxicity* are based on 4 hours tests in laboratory animals. When experimental values are taken from tests using a 1 hour exposure, they can be converted to a 4 hour equivalent by dividing the 1 hour value by a factor of 2 for gases and vapours and 4 for dusts and mists.

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[1] *Guidance on Category 5 Inhalation Values: The OECD Task Force on Harmonisation of Classification and Labelling (HCL) did not include numerical values in Table 3.1.1 above for acute inhalation toxicity class 5 but instead specified doses "equivalent" to the range of 2000-5000 mg/kg bodyweight by the oral or dermal route(see Note (fe) of Table 3.1.1). In some systems, the competent authority may prescribe values.*

3.1.2.6.2 Units for inhalation toxicity are a function of the form of the inhaled material. Values for dusts and mists are expressed in mg/l. Values for gases are expressed in ppmV. Acknowledging the difficulties in testing vapours, some of which consist of mixtures of liquid and vapour phases, the table provides values in units of mg/l. However, for those vapours which are near the gaseous phase, classification should be based on ppmV. As inhalation test methods are updated, the OECD and other test guideline programs will need to define vapours in relation to mists for greater clarity.

3.1.2.6.3 Vapour inhalation values are intended for use in classification of acute toxicity for all sectors. It is also recognised that the saturated vapour concentration of a chemical is used by the transport sector as an additional element in classifying chemicals for packing groups.

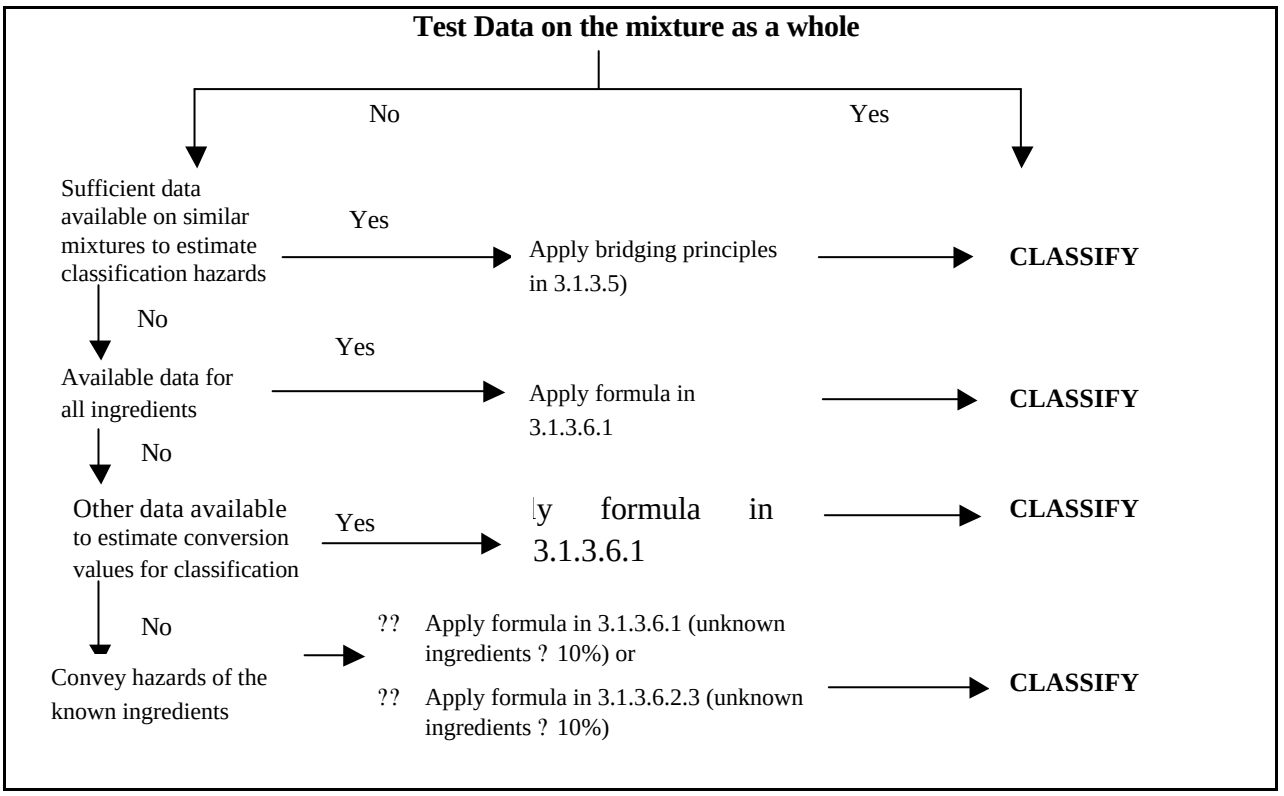
3.1.2.6.4 Of particular importance is the use of well articulated values in the high toxicity categories for dusts and mists. Inhaled particles between 1 and 4 microns mean mass aerodynamic diameter (MMAD) will deposit in all regions of the rat respiratory tract. This particle size range corresponds to a maximum dose of about 2 mg/l. In order to achieve applicability of animal experiments to human exposure, dusts and mists would ideally be tested in this range in rats. The cut-off values in the table for dusts and mists allow clear distinctions to be made for materials with a wide range of toxicities measured under varying tests conditions. The values for dusts and mists should be reviewed in the future to adapt to any future changes in OECD or other test guidelines with respect to technical limitations in generating, maintaining, and measuring dust and mist concentrations in respirable form.

3.1.2.6.5 In addition to classifying for inhalation toxicity, if data are available that indicates that the mechanism of toxicity was corrosivity of the substance or mixture, certain authorities may also label it as *corrosive to the respiratory tract*. Corrosion of the respiratory tract is defined by destruction of the respiratory tract tissue after a single, limited period of exposure analogous to skin corrosion; this includes destruction of the mucosa. The corrosivity evaluation could be based on expert judgment using such evidence as: human or animal experience, existing (*in vitro*) data, pH values, information from similar substances or any other pertinent data.

3.1.3 Classification criteria for mixtures

3.1.3.1 The criteria for substances classify acute toxicity by use of lethal dose data (tested or derived). For mixtures, it is necessary to obtain or derive information that allows the criteria to be applied to the mixture for the purpose of classification. The approach to classification for acute toxicity is tiered, and is dependent upon the amount of information available for the mixture itself and for its ingredients. The flow chart of Figure 3.1.1 below outlines the process to be followed:

Figure 3.1.1: Tiered approach to classification of mixtures for acute toxicity



3.1.3.2 Classification of mixtures for acute toxicity can be carried out for each route of exposure, but is only needed for one route of exposure as long as this route is followed (estimated or tested) for all ingredients. If the acute toxicity is determined for more than one route of exposure, the more severe hazard category will be used for classification. All available information should be considered and all relevant routes of exposure should be identified for hazard communication.

3.1.3.3 In order to make use of all available data for purposes of classifying the hazards of mixtures, certain assumptions have been made and are applied where appropriate in the tiered approach:

(a) The "relevant ingredients" of a mixture are those which are present in concentrations of 1% (w/w for solids, liquids, dusts, mists and vapours and v/v for gases) or greater, unless there is a reason to suspect that an ingredient present at a concentration of less than 1% is still relevant for classifying the mixture for acute toxicity. This point is particularly relevant when classifying untested mixtures which contain ingredients that are classified in Category 1 and Category 2;

~~(b) The acute toxicity estimate (ATE) for an ingredient in a mixture is derived using:~~

- ~~The LD_{50}/LC_{50} where available,~~
- ~~The appropriate conversion value from Table 3.1.2 that relates to the results of a range test for an ingredient, or~~
- ~~The appropriate conversion value from Table 3.1.2 that relates to a classification category of the ingredient;~~

(be) Where a classified mixture is used as an ingredient of another mixture, the actual or derived acute toxicity estimate (ATE) for that mixture may be used when calculating the classification of the new mixture using the formulas in 3.1.3.6.1 and 3.1.3.6.2.3.

Table 3.1.2: Conversion from experimentally obtained acute toxicity range values (or acute toxicity hazard categories) to acute toxicity point estimates for classification for the respective routes of exposure

Exposure routes	Classification category or experimentally obtained acute toxicity range estimate (*see Note 1*)	Converted Acute Toxicity point estimate (*see Note 2*)
Oral (mg/kg bodyweight)	0 < Category 1 ? 5 5 < Category 2 ? 50 50 < Category 3 ? 300 300 < Category 4 ? 2000 *2000 < Category 5 ? 5000*	0.5 5 100 500 2500
Dermal (mg/kg bodyweight)	0 < Category 1 ? 50 50 < Category 2 ? 200 200 < Category 3 ? 1000 1000 < Category 4 ? 2000 *2000 < Category 5 ? 5000*	5 50 300 1100 2500
Gases (ppmV)	0 < Category 1 ? 100 100 < Category 2 ? 500 500 < Category 3 ? 2500 2500 < Category 4 ? 5000 *Category 5 - See footnote to 3.1.2.5.*	10 100 700 3000
Vapours (mg/l)	0 < Category 1 ? 0.5 0.5 < Category 2 ? 2.0 2.0 < Category 3 ? 10.0 10.0 < Category 4 ? 20.0 *Category 5 - See footnote to 3.1.2.5.*	0.05 0.5 3 11
Dust/mist (mg/l)	0 < Category 1 ? 0.05 0.05 < Category 2 ? 0.5 0.5 < Category 3 ? 1.0 1.0 < Category 4 ? 5.0 *Category 5 - See footnote to 3.1.2.5.*	0.005 0.05 0.5 1.5

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

***NOTE 1**: Category 5 is for mixtures which are of relatively low acute toxicity but which under certain circumstances may pose a hazard to vulnerable populations. These mixtures are anticipated to have an oral or dermal LD_{50} value in the range of 2000-5000 mg/kg bodyweight or equivalent dose for other routes of exposure. In light of animal welfare considerations, testing in animals in Category 5 ranges is discouraged and should only be considered when there is a strong likelihood that results of such testing would have a direct relevance for protecting human health.*

***NOTE 2**: These values are designed to be used in the calculation of the ATE for classification of a mixture based on its components and do not represent test results. The values are conservatively set at the lower end of the range of Categories 1 and 2, and at a point approximately 1/10th from the lower end of the range for Categories 3 – 5.*

3.1.3.4 *Classification of mixtures where acute toxicity test data are available for the complete mixture*

Where the mixture itself has been tested to determine its acute toxicity, it will be classified according to the same criteria as those used for substances, presented in Table 3.1.1. If test data for the mixture are not available, the procedures presented below should be followed.

3.1.3.5 *Classification of mixtures where acute toxicity test data are not available for the complete mixture: Bridging principles*

3.1.3.5.1 Where the mixture itself has not been tested to determine its acute toxicity, but there are sufficient data on the individual ingredients and similar tested mixtures to adequately characterise the hazards of the mixture, these data will be used in accordance with the following agreed bridging rules. This ensures that the classification process uses the available data to the greatest extent possible in characterising the hazards of the mixture without the necessity for additional testing in animals.

3.1.3.5.2 *Dilution*

If a mixture is diluted with a substance that has an equivalent or lower toxicity classification than the least toxic original ingredient, and which is not expected to affect the toxicity of other ingredients, then the new mixture may be classified as equivalent to the original mixture. Alternatively, the formula explained in paragraph 3.1.3.6.1 could be applied.

If a mixture is diluted with water or other totally non-toxic material, the toxicity of the mixture can be calculated from test data on the undiluted mixture. For example, if a mixture with an LD50 of 1000 mg/kg bodyweight were diluted with an equal volume of water, the LD50 of the diluted mixture would be 2000 mg/kg bodyweight.

3.1.3.5.3 *Batching*

The toxicity of one production batch of a complex mixture can be assumed to be substantially equivalent to that of another production batch of the same commercial product, and produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the toxicity of the batch has changed. If the latter occurs, new classification is necessary.

3.1.3.5.4 *Concentration of highly toxic mixtures*

If a mixture is classified in Category 1, and the concentration of the ingredients of the mixture that are in Category 1 is increased, the new mixture should be classified in Category 1 without additional testing.

3.1.3.5.5 *Interpolation within one toxicity category*

For three mixtures with identical ingredients, where A and B are in the same toxicity category and mixture C has the same toxicologically active ingredients with concentrations intermediate to the concentrations of those ingredients in mixtures A and B, then mixture C is assumed to be in the same toxicity category as A and B.

3.1.3.5.6 *Substantially similar mixtures*

Given the following:

(a) Two mixtures: (i) A + B
(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;
(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);
(d) Data on toxicity for A and C are available and substantially equivalent, i.e. they are in the same hazard category and are not expected to affect the toxicity of B;

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

3.1.3.5.7 *Aerosols*

An aerosol form of a mixture may be classified in the same hazard category as the tested, non-aerosolised form of the mixture for oral and dermal toxicity provided the added propellant does not affect the toxicity of the mixture on spraying. Classification of aerosolised mixtures for inhalation toxicity should be considered separately.

3.1.3.6 *Classification of mixtures based on ingredients of the mixture (Additivity formula)*

3.1.3.6.1 *Data available for all ingredients*

In order to ensure that classification of the mixture is accurate, and that the calculation need only be performed once for all systems, sectors, and categories, the acute toxicity estimate (ATE) of ingredients should be considered as follows:

- Include ingredients with a known acute toxicity, which fall into any of the GHS acute toxicity categories;
- Ignore ingredients that are presumed not acutely toxic (e.g. water, sugar);
- Ignore ingredients if the oral limit test does not show acute toxicity at 2000 mg/kg bodyweight.

Ingredients that fall within the scope of this paragraph are considered to be ingredients with a known acute toxicity estimate (ATE).

The ATE of the mixture is determined by calculation from the ATE values for all relevant ingredients according to the following formula below for Oral, Dermal or Inhalation Toxic ity:

$$\frac{100}{ATEmix} ? ?_{n} \frac{Ci}{ATE_i}$$

where:

C_i = concentration of ingredient i
n ingredients and i is running from 1 to n
ATE_i = Acute Toxicity Estimate of ingredient i.

3.1.3.6.2 *Data are not available for one or more ingredients of the mixture*

3.1.3.6.2.1 Where an ATE is not available for an individual ingredient of the mixture, but available information such as listed below can provide a derived conversion value, the formula in 3.1.3.6.1 may be applied.

This may include evaluation of:

(a) Extrapolation between oral, dermal and inhalation acute toxicity estimates[2]. Such an evaluation could require appropriate pharmacodynamic and pharmacokinetic data;
(b) Evidence from human exposure that indicates toxic effects but does not provide lethal dose data;
(c) Evidence from any other toxicity tests/assays available on the substance that indicates toxic acute effects but does not necessarily provide lethal dose data; or
(d) Data from closely analogous substances using structure/activity relationships.

This approach generally requires substantial supplemental technical information, and a highly trained and experienced expert, to reliably estimate acute toxicity. If such information is not available, proceed to the provisions of 3.1.3.6.2.3.

3.1.3.6.2.2 In the event that an ingredient without any useable information at all is used in a mixture at a concentration of 1% or greater, it is concluded that the mixture cannot be attributed a definitive acute toxicity estimate. In this situation the mixture should be classified based on the known ingredients only, with the additional statement that x percent of the mixture consists of ingredient(s) of unknown toxicity.

3.1.3.6.2.3 If the total concentration of the ingredient(s) with unknown acute toxicity is ? 10% then the formula presented in 3.1.3.6.1 should be used. If the total concentration of the ingredient(s) with unknown toxicity is ?10%, the formula presented in 3.1.3.6.1 should be corrected to adjust for the total percentage of the unknown ingredient(s) as follows:

$$\frac{100 ? (? C_{unknown} \text{ if } ? 10\%)}{ATEmix} ? ? \sum_{n} \frac{Ci}{ATE_i}$$

3.1.4 Hazard communication

General and specific considerations concerning labelling requirements are provided in *Hazard Communication: Labelling* (Chapter 1.4). Annex 2 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 Categories 1-5 based on the criteria set forth in this chapter.

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[2] *For ingredients with acute toxicity estimates available for other than the most appropriate exposure route, values may be extrapolated from the available exposure route to the most relevant route. Dermal and inhalation route data are not always required for ingredients. However, in case data requirements for specific ingredients include acute toxicity estimates for the dermal and inhalation route, the values to be used in the formula need to be from the required exposure route.*

Table 3.1.3: Acute toxicity label elements

	Category 1	Category 2	Category 3	Category 4	Category 5
Symbol	Skull and crossbones	Skull and crossbones	Skull and crossbones	Exclamation mark	No symbol is used
Signal word	Danger	Danger	Danger	Warning	Warning
Hazard statement: **--Oral**	Fatal if swallowed	Fatal if swallowed	Toxic if swallowed	Harmful if swallowed	May be harmful if swallowed
--Dermal	Fatal in contact with skin	Fatal in contact with skin	Toxic in contact with skin	Harmful in contact with skin	May be harmful in contact with skin
--Inhalation (note 1)	Fatal if inhaled	Fatal if inhaled	Toxic if inhaled	Harmful if inhaled	May be harmful if inhaled

***Note 1**: If the substance/mixture is also determined to be corrosive (based on data such as skin or eye data), corrosivity hazard may also be communicated by some authorities as symbol and/or hazard statement. That is, in addition to an appropriate acute toxicity symbol, a corrosivity symbol (used for skin and eye corrosivity) may be added along with a corrosivity hazard statement such as "corrosive" or "corrosive to respiratory tract".*