Hazard Communication Information Sheet reflecting the US OSHA Implementation of the *Globally Harmonized System (GHS) of Classification and Labelling of Chemicals*

Produced by the SCHC-OSHA Alliance

GHS/HazCom Information Sheet Workgroup

Info Acute Toxicity - Oral *March 2018*

How does OSHA HCS define Oral Acute Toxicity?

Acute toxicity by the oral route refers to those adverse effects occurring following an oral administration of a single dose of a substance, or multiple doses given within 24 hours.

How is Acute Toxicity by the Oral route classified under OSHA's HCS?

Acute toxicity values are expressed as (approximate) LD_{50} (oral) values or as acute toxicity estimates (ATE). The ATE for the classification of a substance is derived using the LD_{50} where available, the appropriate conversion value from the table below that relates to the results of a range test, or the appropriate conversion value from the table below that relates to a classification category.

Table 1: Acute toxicity hazard categories and acute toxicity estimate (ATE) values defining the respective categories

Exposure route	Classification Category			Converted Acute Toxicity point estimate
Oral (mg/kg bodyweight)	0	< Category 1 ≤	5	0.5
	5	< Category 2 ≤	50	5
	50	< Category 3 ≤	300	100
	300	< Category 4 ≤	2000	500

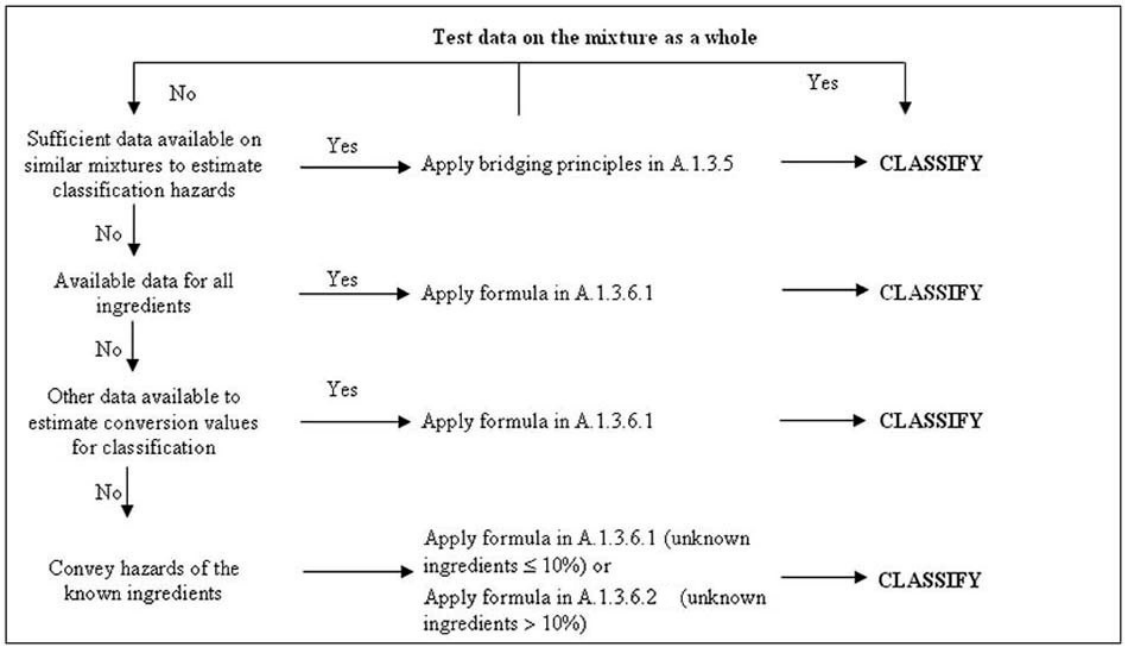
Additional classification considerations

The preferred test species for evaluation of acute toxicity by the oral route is the rat. 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 LD_{50} value from among scientifically validated tests.

Classification criteria for mixtures

Figure 1 on the next page provides the following approach to classification of mixtures for acute toxicity is tiered, and is dependent upon the amount of information available for the mixture itself and for its ingredients. The following flow chart indicates the process that must be followed:

Figure 1: Tiered approach to classification of mixtures for acute toxicity



Classification of mixtures for acute toxicity may be carried out for each route of exposure, but is only required for one route of exposure as long as this route is followed (estimated or tested) for all ingredients and there is no relevant evidence to suggest acute toxicity by multiple routes. When there is relevant evidence of acute toxicity by multiple routes of exposure, classification is to be conducted for all appropriate routes of exposure. All available information shall be considered. The pictogram and signal word used shall reflect the most severe hazard category; and all relevant hazard statements shall be used.

For purposes of classifying the hazards of mixtures in the tiered approach: (a) The "relevant ingredients" of a mixture are those which are present in concentrations ≥ 1% (weight/weight for solids, liquids, dusts, mists and vapors and volume/volume for gases). If there is reason to suspect that an ingredient present at a concentration < 1% will affect classification of the mixture for acute toxicity, that ingredient shall also be considered relevant. Consideration of ingredients present at a concentration < 1% is particularly important when classifying untested mixtures which contain ingredients that are classified in Category 1 and Category 2; (b) Where a classified mixture is used as an ingredient of another mixture, the actual or derived acute toxicity estimate (ATE) for that mixture is used when calculating the classification of the new mixture using the formulas in A.1.3.6.1 and A.1.3.6.2; (c) If the converted acute toxicity point estimates for all ingredients of a mixture are within the same category, then the mixture should be classified in that category. (d) When only range data (or acute toxicity hazard category information) are available for ingredients in a mixture, they may be converted to point estimates in accordance with Table 1 when calculating the classification of the new mixture using the formulas in A.1.3.6.1 and A.1.3.6.2 of 29 CFR 1910.1200.

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 is classified according to the same criteria as those used for substances, presented in Table 1. If test data for the mixture are not available, the procedures presented below must be followed.

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

Where the mixture itself has not been tested to determine its acute toxicity, but there are sufficient data on both the individual ingredients and similar tested mixtures to adequately characterize the hazards of the mixture, these data will be used in accordance with the following bridging principles: Dilution, Batching, Concentration of mixtures, Interpolation within one toxicity category, Substantially similar mixtures, and Aerosols.

A.1.3.6 Classification of mixtures based on ingredients of the mixture (additivity formula)

A.1.3.6.1 *Data available for all ingredients*

The acute toxicity estimate (ATE) of ingredients is considered as follows: (a) Include ingredients with a known acute toxicity, which fall into any of the acute toxicity categories, or have an oral or dermal LD_{50} greater than 2000 but less than or equal to 5000 mg/kg body weight (or the equivalent dose for inhalation); (b) Ignore ingredients that are presumed not acutely toxic (e.g., water, sugar); (c) Ignore ingredients if the data available are from a limit dose test (at the upper threshold for Category 4 for the appropriate route of exposure as provided in the flow chart above) and do not show acute toxicity.

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 toxicity:

$$\frac{100}{ATEmix} = \sum_{n} \frac{Ci}{ATE_i}$$

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

A.1.3.6.2 *Data are not available for one or more ingredients of the mixture*

Where an ATE is not available for an individual ingredient of the mixture, but available information provides a derived conversion value, the formula in A.1.3.6.1 of 29 CFR 1910.1200 may be applied. This information may include evaluation of: (a) Extrapolation between oral, dermal and inhalation acute toxicity estimates. Such an evaluation requires 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 requires substantial supplemental technical information, and a highly trained and experienced expert, to reliably estimate acute toxicity. In the event that an ingredient with unknown acute toxicity is used in a mixture at a concentration ≥ 1%, and the mixture has not been classified based on testing of the mixture as a whole, the mixture cannot be attributed a definitive acute toxicity estimate. In this situation the mixture is classified based on the known ingredients only. (Note: A statement that x percent of the mixture consists of ingredient(s) of unknown toxicity is required on the label and safety data sheet in such cases). If the total concentration of the relevant ingredient(s) with unknown acute toxicity is ≤ 10% then the formula presented in A.1.3.6.1 of 29 CFR 1910.1200 must be used. If the total concentration of the relevant ingredient(s) with unknown acute toxicity is > 10%, the formula presented in A.1.3.6.1 of 29 CFR 1910.1200 is corrected to adjust for the percentage of the unknown ingredient(s) as follows:

$$\frac{100 - (\sum C_{unknown} \text{ if } > 10\%)}{ATE_{mix}} = \sum_{n} \frac{Ci}{ATE_i}$$

Table 2: Acute toxicity by Inhalation Label Elements

Hazard Category	Signal Word and Hazard Statement	Pictogram
Category 1	Danger Fatal if swallowed	 Skull and Crossbones
Category 2	Danger Fatal if swallowed	 Skull and Crossbones
Category 3	Danger Toxic if swallowed	 Skull and Crossbones
Category 4	Warning Harmful if swallowed	 Exclamation Mark

To learn more...

- OSHA: Hazard Communication : https://www.osha.gov/dsg/hazcom/index.html
- SCHC site: http://www.schc.org/osha-alliance

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