

Hazard Communication Standard Contents

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B.6 FLAMMABLE LIQUIDS

B.6.1 Definition

Flammable liquid means a liquid having a flash point of not more than 93°C (199.4°F).

Flash point means the minimum temperature at which a liquid gives off vapor in sufficient concentration to form an ignitable mixture with air near the surface of the liquid, as determined by a method identified in Section B.6.3.

B.6.2 Classification criteria

A flammable liquid shall be classified in one of four categories in accordance with Table B.6.1:

TABLE B.6.1—CRITERIA FOR FLAMMABLE LIQUIDS

Category	Criteria
1	Flash point < 23°C (73.4°F) and initial boiling point ≤ 35°C (95°F)
2	Flash point < 23°C (73.4°F) and initial boiling point > 35°C (95°F)
3	Flash point ≥ 23°C (73.4°F) and ≤ 60°C (140°F)
4	Flash point > 60°C (140°F) and ≤ 93°C (199.4°F)

B.6.3 Additional classification considerations

The flash point shall be determined in accordance with ASTM D56-05, ASTM D3278, ASTM D3828, ASTM D93-08 (incorporated by reference; See §1910.6), or any other method specified in GHS Revision 3, Chapter 2.6.

The initial boiling point shall be determined in accordance with ASTM D86-07a or ASTM D1078 (incorporated by reference; See §1910.6).

C.4.19 FLAMMABLE LIQUIDS
(Classified in Accordance with Appendix B.6)

Pictogram
Flame



Hazard category	Signal word	Hazard statement
1	Danger	Extremely flammable liquid and vapor
2	Danger	Highly flammable liquid and vapor
3	Warning	Flammable liquid and vapor

Precautionary statements

Prevention	Response	Storage	Disposal
<p>Keep away from heat/sparks/open flames/hot surfaces.– No smoking. Chemical manufacturer, importer, or distributor to specify applicable ignition source(s).</p> <p>Keep container tightly closed.</p> <p>Ground/Bond container and receiving equipment <i>- if electrostatically sensitive material is for reloading.</i> <i>- if product is volatile so as to generate hazardous atmosphere.</i></p> <p>Use explosion-proof electrical/ventilating/lighting/.../equipment. ... Chemical manufacturer, importer, or distributor to specify other equipment.</p>	<p>If on skin (or hair): Take off immediately all contaminated clothing. Rinse skin with water/shower.</p> <p>In case of fire: Use ... to extinguish. ... Chemical manufacturer, importer, or distributor to specify appropriate media. <i>- if water increases risk.</i></p>	<p>Store in a well-ventilated place. Keep cool.</p>	<p>Dispose of contents/container to... ... in accordance with local/regional/national/international regulations (to be specified).</p>

Use only non-sparking tools.

Take precautionary measures against static discharge.

Wear protective gloves/eye protection/face protection
Chemical manufacturer, importer, or distributor to specify type of equipment.

C.4.19 FLAMMABLE LIQUIDS (CONTINUED)
(Classified in Accordance with Appendix B.6)

Pictogram
No Pictogram

Hazard category	Signal word	Hazard statement
4	Warning	Combustible liquid

Precautionary statements

Prevention	Response	Storage	Disposal
Keep away from flames and hot surfaces. – No smoking.	In case of fire: Use ... to extinguish. ... Chemical manufacturer, importer, or distributor to specify appropriate media. <i>- if water increases risk.</i>	Store in a well-ventilated place. Keep cool.	Dispose of contents/container to... in accordance with local/regional/national/international regulations (to be specified).
Wear protective gloves/eye protection/face protection Chemical manufacturer, importer, or distributor to specify type of equipment.			

A.8 SPECIFIC TARGET ORGAN TOXICITY SINGLE EXPOSURE

A.8.1 Definitions and general considerations

A.8.1.1 *Specific target organ toxicity - single exposure, (STOT-SE)* means specific, non-lethal target organ toxicity arising from a single exposure to a chemical. All significant health effects that can impair function, both reversible and irreversible, immediate and/or delayed and not specifically addressed in A.1 to A.7 and A.10 of this Appendix are included. Specific target organ toxicity following repeated exposure is classified in accordance with *SPECIFIC TARGET ORGAN TOXICITY – REPEATED EXPOSURE* (A.9 of this Appendix) and is therefore not included here.

A.8.1.2 Classification identifies the chemical as being a specific target organ toxicant and, as such, it presents a potential for adverse health effects in people who are exposed to it.

A.8.1.3 The adverse health effects produced by a single exposure include consistent and identifiable toxic effects in humans; or, in experimental animals, toxicologically significant changes which have affected the function or morphology of a tissue/organ, or have produced serious changes to the biochemistry or hematology of the organism, and these changes are relevant for human health. Human data is the primary source of evidence for this hazard class.

A.8.1.4 Assessment shall take into consideration not only significant changes in a single organ or biological system but also generalized changes of a less severe nature involving several organs.

A.8.1.5 Specific target organ toxicity can occur by any route that is relevant for humans, i.e., principally oral, dermal or inhalation.

A.8.1.6 The classification criteria for specific organ systemic toxicity single exposure are organized as criteria for substances Categories 1 and 2 (See A.8.2.1), criteria for substances Category 3 (See A.8.2.2) and criteria for mixtures (See A.8.3). See also Figure A.8.1.

A.8.2 Classification criteria for substances

A.8.2.1 Substances of Category 1 and Category 2

A.8.2.1.1 Substances shall be classified for immediate or delayed effects separately, by the use of expert judgment on the basis of the weight of all evidence available, including the use of recommended guidance values (See A.8.2.1.9). Substances shall then be classified in Category 1 or 2, depending upon the nature and severity of the effect(s) observed, in accordance with Figure A.8.1.

Figure A.8.1: Hazard categories for specific target organ toxicity following single exposure

<p>CATEGORY 1:</p>	<p>Substances that have produced significant toxicity in humans, or that, on the basis of evidence from studies in experimental animals can be presumed to have the potential to produce significant toxicity in humans following single exposure Substances are classified in Category 1 for STOT-SE on the basis of: (a) reliable and good quality evidence from human cases or epidemiological studies; or (b) observations from appropriate studies in experimental animals in which significant and/or severe toxic effects of relevance to human health were produced at generally low exposure concentrations. Guidance dose/concentration values are provided below (See A.8.2.1.9) to be used as part of weight-of-evidence evaluation.</p>
<p>CATEGORY 2:</p>	<p>Substances that, on the basis of evidence from studies in experimental animals, can be presumed to have the potential to be harmful to human health following single exposure Substances are classified in Category 2 for STOT-SE on the basis of observations from appropriate studies in experimental animals in which significant toxic effects, of relevance to human health, were produced at generally moderate exposure concentrations. Guidance dose/concentration values are provided below (See A.8.2.1.9) in order to help in classification. In exceptional cases, human evidence can also be used to place a substance in Category 2 (See A.8.2.1.6).</p>
<p>CATEGORY 3:</p>	<p>Transient target organ effects There are target organ effects for which a substance does 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 are classified specifically for these effects as discussed in A.8.2.2.</p>
<p><i>Note: The primary target organ/system shall be identified where possible, and where this is not possible, the substance shall be identified as a general toxicant. The data shall be evaluated and, where possible, shall not include secondary effects (e.g., a hepatotoxicant can produce secondary effects in the nervous or gastro-intestinal systems).</i></p>	

A.8.2.1.2 The relevant route(s) of exposure by which the classified substance produces damage shall be identified.

A.8.2.1.3 Classification is determined by expert judgment, on the basis of the weight of all evidence available including the guidance presented below.

A.8.2.1.4 Weight of evidence of all available data, including human incidents, epidemiology, and studies conducted in experimental animals is used to substantiate specific target organ toxic effects that merit classification.

A.8.2.1.5 The information required to evaluate specific target organ toxicity comes either from single exposure in humans (e.g., exposure at home, in the workplace or environmentally), or from studies conducted in experimental animals. The standard animal studies in rats or mice that provide this information are acute toxicity studies which can include clinical observations and detailed macroscopic and microscopic examination to enable the toxic effects on target tissues/organs to be identified. Results of acute toxicity studies conducted in other species may also provide relevant information.

A.8.2.1.6 In exceptional cases, based on expert judgment, it may be appropriate to place certain substances with human evidence of target organ toxicity in Category 2: (a) when the weight of human evidence is not sufficiently convincing to warrant Category 1 classification, and/or (b) based on the nature and severity of effects. Dose/concentration levels in humans shall not be considered in the classification and any available evidence from animal studies shall be consistent with the Category 2 classification. In other words, if there are also animal data available on the substance that warrant Category 1 classification, the chemical shall be classified as Category 1.

A.8.2.1.7 Effects considered to support classification for Category 1 and 2

A.8.2.1.7.1 Classification is supported by evidence associating single exposure to the substance with a consistent and identifiable toxic effect.

A.8.2.1.7.2 Evidence from human experience/incidents is usually restricted to reports of adverse health consequences, often with uncertainty about exposure conditions, and may not provide the scientific detail that can be obtained from well-conducted studies in experimental animals.

A.8.2.1.7.3 Evidence from appropriate studies in experimental animals can furnish much more detail, in the form of clinical observations, and macroscopic and microscopic pathological examination and this can often reveal hazards that may not be life-threatening but could indicate functional impairment. Consequently all available evidence, and evidence relevance to human health, must be taken into consideration in the classification process. Relevant toxic effects in humans and/or animals include, but are not limited to:

(a) Morbidity resulting from single exposure;

(b) Significant functional changes, more than transient in nature, in the respiratory system, central or peripheral nervous systems, other organs or other organ systems, including signs of central nervous system depression and effects on special senses (e.g., sight, hearing and sense of smell);

(c) Any consistent and significant adverse change in clinical biochemistry, hematology, or urinalysis parameters;

- (d) Significant organ damage that may be noted at necropsy and/or subsequently seen or confirmed at microscopic examination;
- (e) Multi-focal or diffuse necrosis, fibrosis or granuloma formation in vital organs with regenerative capacity;
- (f) Morphological changes that are potentially reversible but provide clear evidence of marked organ dysfunction; and,
- (g) Evidence of appreciable cell death (including cell degeneration and reduced cell number) in vital organs incapable of regeneration.

A.8.2.1.8 Effects considered not to support classification for Category 1 and 2

Effects may be seen in humans and/or animals that do not justify classification. Such effects include, but are not limited to:

- (a) Clinical observations or small changes in bodyweight gain, food consumption or water intake that may have some toxicological importance but that do not, by themselves, indicate "significant" toxicity;
- (b) Small changes in clinical biochemistry, hematology or urinalysis parameters and/or transient effects, when such changes or effects are of doubtful or of minimal toxicological importance;
- (c) Changes in organ weights with no evidence of organ dysfunction;
- (d) Adaptive responses that are not considered toxicologically relevant; and,
- (e) Substance-induced species-specific mechanisms of toxicity, i.e., demonstrated with reasonable certainty to be not relevant for human health, shall not justify classification.

A.8.2.1.9 Guidance values to assist with classification based on the results obtained from studies conducted in experimental animals for Category 1 and 2

A.8.2.1.9.1 In order to help reach a decision about whether a substance shall be classified or not, and to what degree it shall be classified (Category 1 vs. Category 2), dose/concentration "guidance values" are provided for consideration of the dose/concentration which has been shown to produce significant health effects. The principal argument for proposing such guidance values is that all chemicals are potentially toxic and there has to be a reasonable dose/concentration above which a degree of toxic effect is acknowledged.

A.8.2.1.9.2 Thus, in animal studies, when significant toxic effects are observed that indicate classification, consideration of the dose/concentration at which these effects were seen, in relation to the suggested guidance values, provides useful information to help assess the need to classify (since the toxic effects are a consequence of the hazardous property(ies) and also the dose/concentration).

A.8.2.1.9.3 The guidance value (C) ranges for single-dose exposure which has produced a significant non-lethal toxic effect are those applicable to acute toxicity testing, as indicated in Table A.8.1.

Table A.8.1: Guidance value ranges for single-dose exposures

Route of exposure	Units	Guidance value ranges for:		
		Category 1	Category 2	Category 3
Oral (rat)	mg/kg body weight	$C \leq 300$	$2000 \geq C > 300$	Guidance values do not apply
Dermal (rat or rabbit)	mg/kg body weight	$C \leq 1000$	$2000 \geq C > 1000$	
Inhalation (rat) gas	ppmV/4h	$C \leq 2500$	$20,000 \geq C > 2500$	
Inhalation (rat) vapor	mg/l/4h	$C \leq 10$	$20 \geq C > 10$	
Inhalation (rat) dust/mist/fume	mg/l/4h	$C \leq 1.0$	$5.0 \geq C > 1.0$	

A.8.2.1.9.4 The guidance values and ranges mentioned in Table A.8.1 are intended only for guidance purposes, i.e., to be used as part of the weight of evidence approach, and to assist with decisions about classification. They are not intended as strict demarcation values. Guidance values are not provided for Category 3 since this classification is primarily based on human data; animal data may be included in the weight of evidence evaluation.

A.8.2.1.9.5 Thus, it is feasible that a specific profile of toxicity occurs at a dose/concentration below the guidance value, e.g., < 2000 mg/kg body weight by the oral route, however the nature of the effect may result in the decision not to classify. Conversely, a specific profile of toxicity may be seen in animal studies occurring at above a guidance value, e.g., ≥ 2000 mg/kg body weight by the oral route, and in addition there is supplementary information from other sources, e.g., other single dose studies, or human case experience, which supports a conclusion that, in view of the weight of evidence, classification is the prudent action to take.

A.8.2.1.10 Other considerations

A.8.2.1.10.1 When a substance is characterized only by use of animal data the classification process includes reference to dose/concentration guidance values as one of the elements that contribute to the weight of evidence approach.

A.8.2.1.10.2 When well-substantiated human data are available showing a specific target organ toxic effect that can be reliably attributed to single exposure to a substance, the substance shall be classified. Positive human data, regardless of probable dose, predominates over animal data. Thus, if a substance is unclassified because specific target organ toxicity observed was considered not relevant or significant to humans, if subsequent human incident data become available showing a specific target organ toxic effect, the substance shall be classified.

A.8.2.1.10.3 A substance that has not been tested for specific target organ toxicity shall, where appropriate, be classified on the basis of data from a scientifically validated structure activity relationship and expert judgment-based extrapolation from a structural analogue that has previously been classified together with substantial support from consideration of other important factors such as formation of common significant metabolites.

A.8.2.2 Substances of Category 3

A.8.2.2.1 Criteria for respiratory tract irritation

The criteria for classifying substances as Category 3 for respiratory tract irritation are:

- (a) Respiratory irritant effects (characterized by localized 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;
- (b) Subjective human observations supported by objective measurements of clear respiratory tract irritation (RTI) (e.g., electrophysiological responses, biomarkers of inflammation in nasal or bronchoalveolar lavage fluids);
- (c) The symptoms observed in humans shall 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 classification for respiratory tract irritation;
- (d) There are currently no scientifically 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; and,
- (e) This special classification will occur only when more severe organ effects including the respiratory system are not observed as those effects would require a higher classification.

A.8.2.2.2 Criteria for narcotic effects

The criteria for classifying substances in Category 3 for narcotic effects are:

- (a) 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; and,

(b) 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, then they shall be considered for classification as Category 1 or 2.

A.8.3 Classification criteria for mixtures

A.8.3.1 Mixtures are classified using the same criteria as for substances, or alternatively as described below. As with substances, mixtures may be classified for specific target organ toxicity following single exposure, repeated exposure, or both.

A.8.3.2 Classification of mixtures when data are available for the complete mixture

When reliable and good quality evidence from human experience or appropriate studies in experimental animals, as described in the criteria for substances, is available for the mixture, then the mixture shall be classified by weight of evidence evaluation of this data. Care shall be exercised in evaluating data on mixtures, that the dose, duration, observation or analysis, do not render the results inconclusive.

A.8.3.3 Classification of mixtures when data are not available for the complete mixture: bridging principles

A.8.3.3.1 Where the mixture itself has not been tested to determine its specific target organ 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 shall be used in accordance with the following bridging principles as found in paragraph A.0.5 of this Appendix: Dilution, Batching, Concentration of mixtures, Interpolation within one toxicity category, Substantially similar mixtures, or Aerosols.

A.8.3.4 Classification of mixtures when data are available for all ingredients or only for some ingredients of the mixture

A.8.3.4.1 Where there is no reliable evidence or test data for the specific mixture itself, and the bridging principles cannot be used to enable classification, then classification of the mixture is based on the classification of the ingredient substances. In this case, the mixture shall be classified as a specific target organ toxicant (specific organ specified), following single exposure, repeated exposure, or both when at least one ingredient has been classified as a Category 1 or Category 2 specific target organ toxicant and is present at or above the appropriate cut-off value/concentration limit specified in Table A.8.2 for Categories 1 and 2, respectively.

Table A.8.2: Cut-off values/concentration limits of ingredients of a mixture classified as a specific target organ toxicant that would trigger classification of the mixture as Category 1 or 2

Ingredients classified as:	Cut-off values/concentration limits triggering classification of a mixture as:	
	Category 1	Category 2
Category 1 Target organ toxicant	≥ 1.0 %	
Category 2 Target organ toxicant		≥ 1.0 %

A.8.3.4.2 These cut-off values and consequent classifications shall be applied equally and appropriately to both single- and repeated-dose target organ toxicants.

A.8.3.4.3 Mixtures shall be classified for either or both single and repeated dose toxicity independently.

A.8.3.4.4 Care shall be exercised when toxicants affecting more than one organ system are combined that the potentiation or synergistic interactions are considered, because certain substances can cause target organ toxicity at < 1% concentration when other ingredients in the mixture are known to potentiate its toxic effect.

A.8.3.4.5 Care shall be exercised when extrapolating the toxicity of a mixture that contains Category 3 ingredient(s). A cut-off value/concentration limit of 20%, considered as an additive of all Category 3 ingredients for each hazard endpoint, is appropriate; however, this cut-off value/concentration limit may be higher or lower depending on the Category 3 ingredient(s) involved and the fact 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 shall be exercised. Respiratory tract irritation and narcotic effects are to be evaluated separately in accordance with the criteria given in A.8.2.2. When conducting classifications for these hazards, the contribution of each ingredient should be considered additive, unless there is evidence that the effects are not additive.

C.4.11 SPECIFIC TARGET ORGAN TOXICITY (Single Exposure)
(Classified in Accordance with Appendix A.8)

Pictogram
Health hazard



Hazard category	Signal word	Hazard statement
1	Danger	Causes damage to organs <...> <<...>> <...> (or state all organs affected if known) <<...>> (state route of exposure if no other routes of exposure cause the hazard)

Precautionary statements

Prevention	Response	Storage	Disposal
<p>Do not breathe dust/fume/gas/mist/vapors/spray. Chemical manufacturer, importer, or distributor to specify applicable conditions.</p> <p>Wash ...thoroughly after handling. ... Chemical manufacturer, importer, or distributor to specify parts of the body to be washed after handling.</p> <p>Do not eat, drink or smoke when using this product.</p>	<p>If exposed: Call a poison center/doctor/... ... Chemical manufacturer, importer, or distributor to specify the appropriate source of emergency medical advice.</p> <p>Specific treatment (see ... on this label) ... Reference to supplemental first aid instruction. <i>- if immediate measures are required.</i></p>	<p>Store locked up.</p>	<p>Dispose of contents/container to... ... in accordance with local/regional/national/international regulations (to be specified).</p>

C.4.11 SPECIFIC TARGET ORGAN TOXICITY (Single Exposure) (CONTINUED)
(Classified in Accordance with Appendix A.8)

Pictogram
Health hazard



Hazard category	Signal word	Hazard statement
2	Warning	May cause damage to organs <...> <<...>> <...> (or state all organs affected, if known) <<...>> (state route of exposure if no other routes of exposure cause the hazard)

Precautionary statements

Prevention	Response	Storage	Disposal
<p>Do not breathe dust/fume/gas/mist/vapors/spray. Chemical manufacturer, importer, or distributor to specify applicable conditions.</p> <p>Wash ... thoroughly after handling. ... Chemical manufacturer, importer, or distributor to specify parts of the body to be washed after handling.</p> <p>Do not eat, drink or smoke when using this product.</p>	<p>If exposed or concerned: Call a poison center/doctor/... ... Chemical manufacturer, importer, or distributor to specify the appropriate source of emergency medical advice.</p>	<p>Store locked up.</p>	<p>Dispose of contents/container to... ... in accordance with local/regional/national/international regulations (to be specified).</p>

C.4.11 SPECIFIC TARGET ORGAN TOXICITY (Single Exposure) (CONTINUED)
(Classified in Accordance with Appendix A.8)

Pictogram
Exclamation mark

Hazard category	Signal word	Hazard statement
3	Warning	May cause respiratory irritation; or May cause drowsiness or dizziness



Precautionary statements

Prevention	Response	Storage	Disposal
<p>Avoid breathing dust/fume/gas/mist/vapors/spray. Chemical manufacturer, importer, or distributor to specify applicable conditions.</p> <p>Use only outdoors or in a well-ventilated area.</p>	<p>If inhaled: Remove person to fresh air and keep comfortable for breathing.</p> <p>Call a poison center/doctor/.../if you feel unwell. ... Chemical manufacturer, importer, or distributor to specify the appropriate source of emergency medical advice.</p>	<p>Store in a well-ventilated place. Keep container tightly closed. <i>- if product is volatile so as to generate hazardous atmosphere.</i></p> <p>Store locked up.</p>	<p>Dispose of contents/container to... ... in accordance with local/regional/national/international regulations (to be specified).</p>