
Gas cylinders — Gases and gas mixtures — Determination of toxicity for the selection of cylinder valve outlets

Bouteilles à gaz — Gaz et mélanges de gaz — Détermination de la toxicité pour le choix des raccords de sortie de robinets

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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For an explanation on the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html.

This document was prepared by ISO/TC 58 *Gas cylinders*, SC 2, *Cylinder fittings*.

This third edition cancels and replaces the second edition (ISO 10298:2010), which has been technically revised.

The main changes compared to the previous edition are as follows:

- The Scope and Clause 4 have been clarified.
- The terms and definitions in Clause 3 have been changed and, in particular, the reference to FTSC codes (that were in ISO 5145) was changed to ISO 14456.
- Some LC50 values have been updated.

Introduction

ISO 5145 specifies the dimensions of different valve outlets for different compatible gas groups. These compatible gas groups are determined according to practical criteria defined in ISO 14456.

These criteria are based on certain physical, chemical, toxic and corrosive properties of the gases. In particular, the tissue corrosiveness is considered in this document.

The aim of this document is to assign for each gas a classification category that takes into account the toxicity by inhalation of the gas. For gas mixtures containing toxic components a calculation based on the method specified in the GHS is proposed.

Since the publication of the first edition of ISO 10298, this International Standard has been used for other purposes than the selection of cylinder valve outlets, e.g. providing toxicity data for the classification of gas and gas mixtures according to the international transport regulations and according to the classification of dangerous substances regulations, which since 2003 is under the umbrella of the Globally Harmonized System (GHS).

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Gas cylinders — Gases and gas mixtures — Determination of toxicity for the selection of cylinder valve outlets

1 Scope

This document lists the best available acute-toxicity data of gases taken from a search of the current literature to allow the classification of gases and gas mixtures for toxicity by inhalation.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

For the purpose of this document, the following terms and definitions apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

- ISO Online Browsing platform: available at <http://www.iso.org/obp>
- IEC Electropedia: available at <http://www.electropedia.org/>

3.1

lethal concentration 50

LC₅₀

concentration of a substance in air exposure to which, for a specified length of time, it is expected to cause the death of 50 % of the entire defined experimental animal population after a defined time period

Note 1 to entry: See [Annex A](#) for the selection of this LC₅₀ value.

3.2

toxicity level

level of toxicity of gases and gas mixtures

Note 1 to entry: In ISO 14456, the toxicity level is divided into three groups:

- Subdivision 1: non toxic [$LC_{50} > 5\,000$ ppm (volume fraction)]
- Subdivision 2: toxic [$200 \text{ ppm (volume fraction)} < LC_{50} \leq 5\,000$ ppm (volume fraction)]
- Subdivision 3: very toxic [$LC_{50} \leq 200$ ppm (volume fraction)]

These subdivisions are sometimes used in transport regulations.

where

LC₅₀ values correspond to 1 h exposure to gas;

ppm (volume fraction) indicates parts per million, by volume.

Note 2 to entry: In the GHS, the inhalation toxicity levels are:

Category 1: Fatal if inhaled	0 ppm < LC ₅₀ ≤ 100 ppm (volume fraction)
Category 2: Fatal if inhaled	100 ppm (volume fraction) < LC ₅₀ ≤ 500 ppm (volume fraction)
Category 3: Toxic if inhaled	500 ppm (volume fraction) < LC ₅₀ ≤ 2 500 ppm (volume fraction)
Category 4: Harmful if inhaled	2 500 ppm (volume fraction) < LC ₅₀ ≤ 20 000 ppm (volume fraction)

Note 3 to entry: In GHS, the LC₅₀ values correspond to 4 hours exposure. Consequently, the LC₅₀ values given in [Annex B](#) (see [4.2.2](#)) need to be divided by 2 (i.e. $\sqrt{4/1}$). The reasoning behind the division by 2 is given in [A.2](#).

3.3 lethal dose 50

LD₅₀

amount of a material, given all at once, which causes the death of 50 % of a group of test animals

3.4 lethal concentration low value

LC_{Lo}

lowest concentration of a substance in air, other than the LC₅₀, which was reported in the original reference paper as having caused death in humans or animals

4 Determination of toxicity

4.1 General

Toxicity may be determined through a test method ([4.2](#)) for gas mixtures where the data for the components exist, or through a calculation method ([4.3](#)).

For reasons of animal welfare, inhalation toxicity tests geared only for the classification of gas mixtures should be avoided if the toxicity of each of the components is available. In this case, toxicity is determined in accordance with [4.3](#).

4.2 Test method

4.2.1 Test procedure

When new toxicity data are being considered for inclusion in this document, an internationally recognized test method such as OECD TG 403 ([4.3](#)) should be used.

NOTE For this document, LC₅₀ is equivalent to 1 h exposure to albino rats.

4.2.2 Results for pure gases

The toxicity of pure gases is listed in [Annex B](#), in which LC₅₀ values correspond to 1 h exposure. Some of these values have been estimated in accordance with [Annex A](#).

4.3 Calculation method

The LC₅₀ value of a gas mixture is calculated using [Formula 1](#):

$$LC_{50i} = \frac{1}{\sum_i \frac{C_i}{LC_{50}}} \quad (1)$$

where

C_i is the mole fraction of the i th toxic component present in the gas mixture;

LC_{50i} is the lethal concentration of the i th toxic component [LC₅₀ < 5 000 ppm (by volume)].

After the LC_{50} of the gas mixture has been calculated, this mixture is classified in accordance with [3.2](#).

NOTE Potential synergistic effects are not considered in Formula 1.

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Annex A (informative)

Selection of an LC₅₀ value for a particular gas

A.1 General

When collecting data from the open literature on the acute inhalation toxicity of gases, some difficulties are experienced. For example, taking into account the very early years of publication, one cannot expect to get results of standardized tests. Moreover, data from reporting sources have to be validated with respect to their details in handling and summarizing information. Furthermore, there is a lack of information on inhalation toxicity for several gases. Thus, particular attention is needed to incorporate all the available facts to complete the toxicological characteristics of gases.

A.2 Time adjustment

In inhalation toxicity tests, the dose-response relationship can be described by [Formula A.1](#):

$$W = c \cdot t \quad (\text{A.1})$$

where

W is a constant which is specific for any given effect, e.g. the deaths of 50 % of the animals exposed;

$c \cdot t$ is the applied dose expressed as the product of concentration and exposure time.

This equation, called Haber's rule, is applicable as long as the biological half-life of the substance in question is reasonably longer than the exposure time.

For gases and vapours with appreciable rates of detoxification or excretion over the time in question, it was found that the relationship between concentration and time is better described by [Formula A.2](#).

$$W = c \cdot t^{0,5} \quad (\text{A.2})$$

When extrapolating from 4 h to 1 h, Formula A.2 predicts lower LC₅₀ values than does Haber's rule. To be on the safe side this principle was applied by the UN Transport Recommendations in adopting the conversion factor 2 (i.e. $\sqrt{4/1}$) to allow classification of materials on the basis of 1 h LC₅₀ data. On the other hand, Haber's rule predicts a lower LC₅₀ when going from a 1-h to a 4-h LC₅₀. To make use of all the available data on acute inhalation toxicity under the different exposure schemes, a more generalized version was applied.

Using 1 h as the point of reference,

- going up from shorter periods, linear extrapolation was preferred;
- coming down from longer periods, the conversion factor $\sqrt{x \text{ h} / 1 \text{ h}}$ was used.

However, test results for a period less than 0,5 h were not used, as this was deemed unreliable.

A.3 Choice of animal

Since data on humans, if available, are usually not sufficient to derive any dose-response relationship, laboratory animals are used to investigate the toxicity of substances on warm-blooded animals.

Unless there are counter indications, such as extraordinarily high or low susceptibility of the rat compared to other animals or humans, the rat is the preferred species in the most common toxicity tests. Therefore, LC₅₀ data in rats are the most likely to be found. If they are missing, data from animals close to the rat in body weight are evaluated.

A.4 Adjustment for effects

Instead of LC₅₀, often the term LC_{L0} is found in the reporting literature and in databases.

Unfortunately, the use of this term is not consistent enough to make any assumptions as to whether the LC₅₀ is below or above that value. Nevertheless, it seems reasonable to make the same use of the LC_{L0} as if it were information about an approximate lethal concentration (ALC). For the classification of gases, no higher precision is required, but the calculation formula for gas mixtures requires a definite LC₅₀ value to be set. Another LC value has been taken as LC₅₀ when additional information proved it plausible to do so.

A.5 Read across

Some substances had to be characterized as analogous to chemically related structures with known physiological properties. Structure-activity relationships have been taken into consideration as far as possible. Moreover, in several instances, the toxicological impact on the respiratory tract is based on fundamental reactions such as the hydrolysis of different gases in the presence of moisture leading to the same reactive principle.

A.6 Other routes of application

This route may only be used as a very last option.

Sometimes the inhalation toxicity of volatile liquids has to be assessed on the basis of other parenteral, especially intraperitoneal (i.p.), LD₅₀ values. There is a good correlation between the LC₅₀ and LD₅₀ i.p. as far as systemically active substances are concerned. Taking toxic pesticides as an example, it could be shown that an LD₅₀ i.p. corresponds in aerosol studies by far and large with the same body weight-related dose inhaled by rats during a 4-h period. For instance, an LD₅₀ i.p. of 100 mg/kg can be assumed to be equivalent to a 4 h-LC₅₀ of about 1 mg/litre air.

A.7 Conclusion

The selection of an LC₅₀ value for a particular gas follows the logic algorithm shown in [Figure A.1](#). The preferred measurement standard is LC₅₀ RAT for 1 h. Lacking good data for these exact parameters, LC₅₀ RAT values for times different from, but closest to, 1 h were selected, eliminating all data for exposures less than 0,5 h. If no reliable LC₅₀ data from RAT were available, the next animal of choice was MUS (mouse), then in the following order: rabbit, guinea-pig, cat, dog, and monkey. Data for 1 h exposures were preferred. If no reliable LC₅₀ data were found for any animal, then a search was made for a reliable LC_{L0} value, utilizing the same hierarchy of animals.

If no reliable LC₅₀ or LC_{L0} value was obtainable, a value was provisionally allocated based on any one, a combination, or all of the following:

- a) reaction (decomposition) of the product in air;
- b) analogy to similar products;



Annex B (informative)

LC₅₀ values for toxic gases and toxic vapours used in gas mixtures

[Table B.1](#) lists for each gas the LC₅₀ values and the literature references.

[Table B.2](#) lists for each vapour the LC₅₀ values and the literature references.

Table B.1 — List of toxic gases with their LC₅₀ values and literature sources

Gases Common name	CAS ^a No.	UN No.	LC ₅₀ ^b /1 h ppm (volume fraction)	Remarks	Literature reference (see the Bibliography)
Ammonia	7664-41-7	1005	7 338		[2]
Arsine	7784-42-1	2188	178		[62]
Arsenic pentafluoride	7784-36-3	3308	178	By analogy with arsine	—
Boron trichloride	10294-34-5	1741	2 541		[2]
Boron trifluoride	7637-07-2	1008	864		[42]
Bromine chloride	13863-41-7	2901	290	Estimated from chlorine	—
Carbon monoxide	630-08-0	1016	3 760	Time-adjusted	[6]
Carbonyl fluoride	353-50-4	2417	360		[5]
Carbonyl sulfide	463-58-1	2204	1 700	Time-adjusted	[7]
Chlorine	7782-50-5	1017	293		[2]
Chlorine pentafluoride	13637-63-3	2548	122		[8]
Chlorine trifluoride	7790-91-2	1749	299		[8]
Chlorotrifluoroethylene	79-38-9	1082	2 000	Time-adjusted	[10]
Chloromethane	74-87-3	1063	5 133		[54]
Cyanogen	460-19-5	1026	350		[11]
Cyclopropane	75-19-4	1027	220 000	"Non-toxic" – LC _{LO} ^c – Mouse – Time-adjusted	—
Cyanogen chloride	506-77-4	1589	80	Time-adjusted	[12]
Deuterium chloride	7698-05-7	1789	3 120		—
Deuterium selenide	13536-95-3	2202	51	Same as hydrogen selenide	—
Deuterium sulfide	13536-94-2	1053	712	Same as hydrogen sulfide	—
Diborane	19287-45-7	1911	80	Time-adjusted	[13]
Dichlorosilane	4109-96-0	2189	314		[52]
Dimethylamine	124-40-3	1032	5 290	Time-adjusted	[67]
Dinitrogen trioxide	10544-73-7	2421	57	Calculated from decomposition into NO ₂	—
Ethylene oxide	75-21-8	1040	2 900	Time-adjusted	[18]

^a CAS = Chemical Abstract System.

^b See 3.2.2.

^c LC_{LO} = lethal concentration low value.

Table B.1 (continued)

Gases Common name	CAS ^a No.	UN No.	LC ₅₀ ^b /1 h ppm (volume fraction)	Remarks	Literature reference (see the Bibliography)
Fluorine	7782-41-4	1045	185		[19]
Fluorine	7782-41-4	1045	185		[19]
Germane	7782-65-2	2192	620		[55]
Hexafluoroacetone	684-16-2	2420	470	Time-adjusted	[56]
Hydrogen bromide	10035-10-6	1048	2 860		[51]
Hydrogen chloride	7647-01-0	1050	2 810		[45]
Hydrogen iodide	10034-85-2	2197	2 860	By analogy with hydrogen bromide	—
Hydrogen selenide	07783-07-5	2202	51		[57]
Hydrogen sulfide	07783-06-4	1053	712		[2]
Hydrogen telluride	07783-09-7	3160	51	By analogy with hydrogen selenide	
Methyl bromide	74-83-9	1062	850	Time-adjusted	[23]
Methylchlorosilane	993-00-0	2534	2 810	Adjusted for HCl equivalent	[53]
Methyl mercaptan	74-93-1	1064	1 350	Time-adjusted	[24]
Methyl vinyl ether (inhibited)	107-25-5	1087	>40 000	Unverified source at 64 000 ppm	—
Monoethylamine	75-04-7	1036	16 000	Time-adjusted	[25]
Monomethylamine	74-89-5	1061	7 110		[46]
Nitrogen monoxide	10102-43-9	1660	115	Same as nitrogen dioxide	—
Nitrogen dioxide	10102-44-0	1067	115		[28]
Nitrogen trifluoride	7783-54-2	2451	6 700		[48]
Nitrosyl chloride	2696-92-6	1069	35	Time-adjusted – LC _{LO} – cat	[29]
Oxygen difluoride	7783-41-7	2190	2,6		[8]
Ozone	10028-15-6		9	Time-adjusted	[30]
Phosgene	75-44-5	1076	5	Time-adjusted	[32]
Phosphine	7803-51-2	2199	20	Time-adjusted	[64]
Phosphorus pentafluoride	07647-19-0	2198	261	Derived from decomposition to HF	—
Phosphorus trifluoride	7783-55-3	3308	436	Derived from decomposition to HF	—
Selenium hexafluoride	7783-79-1	2194	50	Time-adjusted	[39]
Silane	7803-62-5	2203	19 000	Time-adjusted	[2]
Silicon tetrafluoride	7783-61-1	1859	922		[5]
Stibine	7803-52-3	2676	178	By analogy with arsine	—
Sulfur dioxide	7446-09-5	1079	2 520		[35]

^a CAS = Chemical Abstract System.

^b See 3.2.2.

^c LC_{LO} = lethal concentration low value.

Table B.1 (continued)

Gases Common name	CAS ^a No.	UN No.	LC ₅₀ ^b /1 h ppm (volume fraction)	Remarks	Literature reference (see the Bibliography)
Sulfur tetrafluoride	7783-60-0	2418	40		[36]
Sulfuryl fluoride	2699-79-8	2191	3 020		[2]
Tellurium hexafluoride	7783-80-4	2195	25	Time-adjusted	[39]
Tetrafluoroethylene	116-14-3	1081	2 000		—
Trifluoroacetyl chloride	354-32-5	3057	10	Similar to trichloroacetyl chloride	—
Trifluoroethylene	359-11-5	1954	2 000	Time-adjusted Taken from chlorotrifluoroethylene	—
Trimethylamine	75-50-3	1083	7 000	LC _{LO} – Time-adjusted	[66]
Tungsten hexafluoride	7783-82-6	2196	218	Derived from decomposition to HF	—
Vinyl bromide (inhibited)	593-60-2	1085	>40 000		—
Vinyl chloride (inhibited)	75-01-4	1086	150 000		[47]
Vinyl fluoride (inhibited)	75-02-5	1860	>40 000		—
^a CAS = Chemical Abstract System. ^b See 3.2.2. ^c LC _{LO} = lethal concentration low value.					

Table B.2 — List of toxic liquefiable vapours with their LC₅₀ values and literature sources

Vapours Common name	CAS ^a No.	UN No.	LC ₅₀ ^b /1 h ppm (volume fraction)	Remarks	Literature reference (see the Bibliography)
Antimony pentafluoride	7783-70-2	1732	30	Mouse	[3]
Arsenic trifluoride	7784-35-2	1556	178	By analogy with arsine	—
Bis(trifluoromethyl) peroxide	927-84-4		10	Assumed (conservative)	—
Boron tribromide	10294-33-4	2692	950	Derived from HBr with BF ₃	—
Bromine chloride	13863-41-7	2901	290	Estimated from chlorine	—
Bromine pentafluoride	7789-30-2	1745	25	Time- and effect-adjusted	—
Bromine trifluoride	7787-71-5	1746	180	Estimated from F ₂	—
Bromoacetone	598-31-2	1569	260	By analogy with chloroacetone	—
Deuterium fluoride	14333-26-7		1 100		—
Dibromodifluoromethane	1868-53-7	1941	27 000	LC _{LO} – Time-adjusted	—
^a CAS = Chemical Abstract System. ^b See 4.2.2. ^c According to the definition this is a gas but for transport regulations, it has always been considered as a liquid.					

Table B.2 (continued)

Vapours Common name	CAS ^a No.	UN No.	LC ₅₀ ^b /1 h ppm (volume fraction)	Remarks	Literature reference (see the Bibliography)
Dichloro(2-chlorovinyl)arsine			8	Extrapolated from intravenous injection	[14]
Diethylamine	109-89-7	1154	8 000	Time adjusted	[67]
Diethylzinc	557-20-0		non-toxic	Assumed (conservative)	[70]
Diphosgene	503-38-8		2	Derived from phosgene (conservative)	—
Ethylchloroarsine	598-14-1	1892	7	LC _{LO} – Human – Time-adjusted	[17]
Heptafluorobutyronitrile	375-00-8		10	Assumed (conservative)	—
Hydrogen cyanide	74-90-8	1613	144	Time-adjusted	[59]
Hydrogen fluoride ^c	7664-39-3	1052	1 307	Median value of 5 studies	[61]
Iodine pentafluoride	7783-66-6	2495	120	Similar to ClF ₅	—
Methyldichloroarsine	593-89-5	1556	7	By analogy with ethyldichloroarsine	—
Methyldichlorosilane	75-54-7	1242	1 785		[49]
Nickel carbonyl	13463-39-3	1259	20	Time-adjusted	[27]
Pentaborane	19624-22-7	1380	10	Time-adjusted	[31]
Pentafluorobutyronitrile	None listed		10		—
Pentafluoropropionitrile	422-04-8		10	Assumed (conservative)	—
Perchloryl fluoride	7616-94-6		770	Time-adjusted	[12]
Perfluorobut-2-ene	360-89-4		12 000	“Non-toxic” – LC _{LO} – Time-adjusted	[3]
Phenylcarbylamine chloride	622-44-6	1672	5	By analogy with phosgene	—
Propylene oxide	75-56-9	1280	7 140	Time-adjusted	[60]
Silicon tetrachloride	10026-04-7	1818	1 312		[49]
Tellurium hexafluoride	7783-80-4	2195	25	Time-adjusted	[39]
Tetraethyl lead	78-00-2	1649	63		[37]
Tetrafluorohydrazine	10036-47-2		100	Time-adjusted	[38]
Tetramethyl lead	75-74-1		800	Time-adjusted	[65]
Thionyl chloride	7719-09-7	1836	500		[58]
Trichlorosilane	10025-78-2	1295	2 780		[50]
Triethylaluminium	97-93-8		non-toxic	Assumed (conservative)	[70]
Triethylborane	97-94-9		1 400	Time-adjusted	[13]

^a CAS = Chemical Abstract System.

^b See 4.2.2.

^c According to the definition this is a gas but for transport regulations, it has always been considered as a liquid.

Table B.2 (continued)

Vapours Common name	CAS ^a No.	UN No.	LC ₅₀ ^b /1 h ppm (volume fraction)	Remarks	Literature reference (see the Bibliography)
Trifluoroacetonitrile	353-85-5		500	Time- and effect- adjusted; taken from trichloroacetonitrile	—
Trimethylstibine			178	By analogy with stibine	—
Uranium hexafluoride	7783-81-5	2978	25	By analogy with tellurium hexafluoride	—
^a CAS = Chemical Abstract System. ^b See 4.2.2. ^c According to the definition this is a gas but for transport regulations, it has always been considered as a liquid.					