INTERNATIONAL STANDARD

ISO 10298

Third edition
2018-02

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

Reference number
ISO 10298:2018(E)

ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Fax: +41 22 749 09 47
Email: copyright@iso.org
Website: www.iso.org

Published in Switzerland

Contents

Page

Foreword ..... **iv**

Introduction ..... **v**

1 Scope **1**

2 Normative references **1**

3 Terms and definitions **1**

4 Determination of toxicity **2**

4.1 General 2

4.2 Test method 2

4.2.1 Test procedure 2

4.2.2 Results for pure gases 2

4.3 Calculation method 2

Annex A (informative) **Selection of an LC_{50} value for a particular gas** **4**

Annex B (informative) **LC50 values for toxic gases and toxic vapours used in gas mixtures** **7**

Bibliography **12**

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).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

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).

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
LC_{50}
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 LC_{50} 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 ppm (volume fraction) < LC_{50} ≤ 5 000 ppm (volume fraction)]

— Subdivision 3: very toxic [LC_{50} ≤ 200 ppm (volume fraction)]

These subdivisions are sometimes used in transport regulations.

where

LC_{50} 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 LC_{50} 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
LD_{50}
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 LC_{50}, 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[43] should be used.

NOTE For this document, LC_{50} 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 LC_{50} values correspond to 1 h exposure. Some of these values have been estimated in accordance with Annex A.

4.3 Calculation method

The LC_{50} 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 ith toxic component present in the gas mixture;

LC_{50i} is the lethal concentration of the ith toxic component [LC_{50} < 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.

Annex A
(informative)

Selection of an LC_{50} 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:

$$W = c \cdot t \tag{A.1}$$

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.

$$W = c \cdot t^{0,5} \tag{A.2}$$

When extrapolating from 4 h to 1 h, Formula A.2 predicts lower LC_{50} 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 LC_{50} data. On the other hand, Haber's rule predicts a lower LC_{50} when going from a 1-h to a 4-h LC_{50}. 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, LC_{50} 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 LC_{50}, often the term LC_{LO} 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 LC_{50} is below or above that value. Nevertheless, it seems reasonable to make the same use of the LC_{LO} 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 LC_{50} value to be set. Another LC value has been taken as LC_{50} 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.), LD_{50} values. There is a good correlation between the LC_{50} and LD_{50} i.p. as far as systemically active substances are concerned. Taking toxic pesticides as an example, it could be shown that an LD_{50} 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 LD_{50} i.p. of 100 mg/kg can be assumed to be equivalent to a 4 h-LC_{50} of about 1 mg/litre air.

A.7 Conclusion

The selection of an LC_{50} value for a particular gas follows the logic algorithm shown in Figure A.1. The preferred measurement standard is LC_{50} RAT for 1 h. Lacking good data for these exact parameters, LC_{50} 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 LC_{50} 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 LC_{50} data were found for any animal, then a search was made for a reliable LC_{LO} value, utilizing the same hierarchy of animals.

If no reliable LC_{50} or LC_{LO} 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;