

**Committee of Experts on the Transport of Dangerous Goods  
and on the Globally Harmonized System of Classification  
and Labelling of Chemicals**

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**Sub-Committee of Experts on the Transport of  
Dangerous Goods**

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Item 5 (b) of the provisional agenda

**Transport of gases: Miscellaneous**

**LC50 Values in P200 related to ST/SG/AC.10/C.3/2020/8**

**Transmitted by European Industrial Gases Association (EIGA)**

**Introduction**

1. This paper provides responses to some comments of delegations during the Sub-Committee of Experts' virtual session in June 2020, concerning document ST/SG/AC.10/C.3/2020/8 Update of LC50 Values in P200.

For internal reasons, EIGA can no longer take a position on the LC50 for ammonia. As a result, EIGA distances itself from the ammonia sections in ST/SG/AC.10/C.3/2020/8.

EIGA continues to remain with its proposed LC50 values for Boron Trifluoride, Tungsten Hexafluoride, Phosphorous Pentafluoride and Hydrogen Fluoride (anhydrous).

**Comments and Responses**

**C1.** Only changes are proposed in which the value for the LC50 becomes higher. Are there cases where the inverse has been concluded?

**R1.** The LC50 that are given in the UN Model Regulations have been for the most part copied since many years from standard ISO 10298:1995. The current values given in the UN Model Regulation are aligned with ISO 10298:1995.

We have identified only those 5 values where the data of P200 and ISO 10298 were not aligned. There are no reverse cases.

**C2.** For UN 1052 HYDROGEN FLUORIDE, ANHYDROUS, the new proposed LC50 value is calculated as median value from multiple studies. We do not support using the median LC50 if there are multiple studies and multiple LC50 values available. As the classification is based on extrapolation from an animal study to a human, a conservative approach is necessary to take into account the inter-species and intra-species variability. Therefore, the most conservative value from the available reliable studies should be chosen. This is the same approach that is followed in the document for UN 1005 AMMONIA, ANHYDROUS, where the most conservative result has been selected.

**R2.** ISO/TC58/SC2/WG7 believes that the 966 ppm LC50 value for hydrogen fluoride, which was included in ISO 10298 previous versions, is not the most appropriate value to use.

The most appropriate LC50 value to adopt for hydrogen fluoride is the value from the most technically sound study.

The more recent hydrogen fluoride studies, which were not publicly available when ISO 10298:1995 was adopted, are technically better than the older studies for the following reasons:

- They employed a better exposure method (head-only vs. whole body). With whole-body exposures, it is much more difficult to achieve accurate and reproducible concentrations in the breathing zone. Furthermore, the total exposure is often underestimated because the animals are simultaneously exposed via the dermal and oral routes (via grooming). The new OECD inhalation test guidelines support this position:

For acute inhalation toxicity studies, the preferred mode of exposure is the head/nose-only exposure technique. This type of exposure minimizes exposure or uptake by non-inhalation routes. Additionally, it allows testing of high concentrations as required to meet the limit concentration. The instability of test compounds (e.g., reactivity with excreta or humidity) and the possible heterogeneity of the test atmosphere in inhalation chambers are of less concern when head/nose-only inhalation chambers are used. The duration required to attain the inhalation chamber equilibration is minimal in head/nose-only chambers.

- The more recent studies used improved analytical methods:

Sampling and analytical methods used in the human and animal studies conducted in the 1960s and 1970s were not as sensitive as those perfected by the late 1980s and 1990s and may have under- or over-estimated concentrations. An improved sampling/analytical methodology developed by Haskell.

Laboratory (1990) indicates that HF may have collected on glassware in the exposure apparatus. That factor would indicate that exposure concentrations in the early studies may have been underestimated.

- Newer studies are more likely to have been conducted in accordance with GLPs.

Based on these technical points, WG 7 believed that the most appropriate value for hydrogen fluoride is the Haskell (1990) LC50 value of 2300 ppm. This is also supported by the Dalbey et al. (1998) work showing the LC50 to be > 2039 ppm.

A statistical approach applying equal weight to all of the available studies could also be used to select the LC50 value to adopt. There are five 1-hour rat LC50 values in the AEGL document to consider. Three of these values are virtually identical as indicated in the 2004 AEGL report:

Similar 1-hour LC50 values for the rat were found by Wohlslagel et al. (1976), Rosenholtz et al. (1963), and MacEwen and Vernot (1970); 1395, 1307, and 1276 ppm, respectively.

Finally, the mean of the five LC50 values is 1,449 ppm, and the median LC50 value is 1307 ppm. This is why, WG7 proposes that the median LC50 of 1307 ppm be adopted for hydrogen fluoride as a reasonable value.

**C3.** The changes proposed to UN 2196 and UN 2198 are presented as consequential amendments due to the change in LC50 value for UN 1052. In the case the LC50 value for UN 2196 and UN 2198 is above 200 ppm, the proposed amendments have consequences for packing instruction P200. These gases would then be allowed to be transported with a pressure relief device, since they would pass the 200 ppm criterium. This would need to be made clear in the proposal.

**R3.** This is noted.

**C4.** Concerning UN 1005 AMMONIA, ANHYDROUS, the proposed changes in LC50 are in line with the presented toxicity data. However, the implications of this change are not clear. If ammonia is no longer assigned to Class 2.3 based on an LC50 value < 5000 ppm, other information must be provided to support its assignment into Class 2.3 as a corrosive gas. This information is not presented in the paper, while in paragraph 8 of the document, it is stated that "This gas is corrosive to human tissue at low concentrations ... ". We would like to see the data on which this statement is based. This would be necessary in order to classify mixtures containing ammonia, as well as to promote harmonization in the chemical supply chain and oversee the implications of this change.

**R4.** For internal reasons, EIGA can no longer take a position on the LC50 for ammonia. As a result, EIGA distances itself from the ammonia sections in ST/SG/AC.10/C.3/2020/8.

**C5.** There is a concern on indicating that anhydrous ammonia no longer meets the criteria for toxic gases (even though a general provision exists to include it in Division 2.3). We believe that a special provision associated to UN 1005, ANHYDROUS AMMONIA, indicating that this gas is toxic based on its corrosivity could be beneficial.

**R5.** For internal reasons, EIGA can no longer take a position on the LC50 for ammonia. As a result, EIGA distances itself from the ammonia sections in ST/SG/AC.10/C.3/2020/8.

**C6.** Is the exposure time for the inhalation LC50 value of UN 1008 (BORON TRIFLUORIDE) for 1h or 4h? It is helpful to evaluate the impact on the GHS classification of relevant substances.

**R6.** It is one-hour, as defined in the UN Model Regulations.

**C7.** It would have been interesting to have the LC50 values mentioned in point 19.

**R7.** This is noted.

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