



Chemically Speaking LLC

26 Casper Berger Road
Whitehouse Station, NJ 08889
www.chemicallyspeakingllc.com

Oct 28, 2019

Hervé Barthélémy
Convenor of ISO/TC 58/SC 2/WG 7
herve.barthelemy@airliquide.com

Subject: Complementary information regarding LC50 for Ammonia (N212) and LC 50 comparison table for gases covered by the Resolution (N211)

I apologize for the delay in responding to your e-mail of Oct 17, 2019 seeking to prepare a Comparison table for the LC₅₀s (ISO 10298/CGA P-20:2017/UN/EIGA doc. 169/17) of the gases concerned by the Resolution taken at the last ISO/TC 58/SC 2 meeting as well as values for Ammonia. I have been traveling extensively and have only gotten back to my office to review my old files.

The following are my thoughts on these. Some information may have been stated elsewhere or previous correspondence, but I feel that it is worthwhile to repeat it for clarity.

Ammonia

I'm not sure where the CGA value of 3,669 ppm came from. As noted in my Sept 24, 2015 letter to Jack Wert and Jill Thompson, CGA, "A History on the development of CGA P-20 and ISO 10298" (see attached), Jay Harding of Air Liquide led the CGA effort to develop CGA P-20. Dr. Carol Maslansky, GeoEnvironmental Consultants Inc. gathered, reviewed and commented on the various LC₅₀ studies for the P-20 Committee.

In Jay Harding and Doug Bonnar's report to the Specialty Gases Committee on Jan 2, 1990 a LC₅₀ of 14,070 ppm was listed for Ammonia. This was based on the study by Appleman, et. al in 1982. See the attached review sheet (attachment 3) Ammonia 16,600 ppm in which Dr. Carol Maslansky concluded that the study was flawed due to use of variable exposure times. Also 100% of the males died at 11,000 ppm while no females died. She proposed a conservative value of 14,070 ppm based on the male and female data.

Another study Ammonia 4,230 ppm only involved 12 male mice. Dr. Carol Maslansky commented that this was close to Vernot's 4,837 ppm for mice. She rejected it because mice have smaller lung capacity than rats and the study was only done with males. See attachment 1

The review on Ammonia 7,338 ppm by Vernot, was also rejected since only 5 male rats were used. See attachment 2. Jay Harding was able to contact Vernot in 1992 and reported in a letter to DOT in May 1992

Table 5. CGA and ISO agree on the data for 19 materials which appear here. For Ammonia we believe Vernot has the best data. We have spoken with Mr. Vernot who now lives in Maryland and works at the American Petroleum Institute in Washington. His work while at University of California at Irvine was high grade and produced reliable data. For the most part wherever we had one hour LC₅₀ RAT data from Vernot, we accepted that above others. For Boron Trichloride Vernot has appropriate data, rather than an LCLO value. For Boron Trifluoride our data from Vernot is solid and is more conservative than DOT. For Carbonyl Sulfide and Chlorine Trifluoride we have reliable RAT data

I'm not sure whether Dr. Carol Maslansky agreed with this position.



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Hydrogen Fluoride

The Hydrogen Fluoride LC₅₀ value was discussed in detail during the TC58 SC2 WG7 2007 and 2008 meetings. We concluded that the value should be the median value (1,307 ppm) of the 5 values from Table 3-4 of the 2004 US National Advisory Committee AEGL review for Hydrogen Fluoride. This was summarized in the letter from Carrie Hamilton and myself to Dr. Sylvie Tissot Jan 28, 2008. This should be referenced for clarity along with

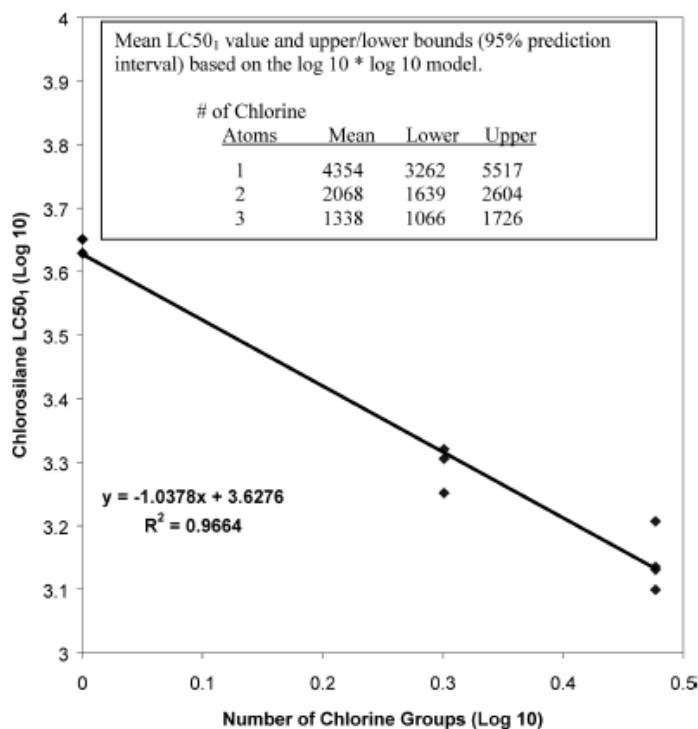
61- Acute Exposure Guideline Levels for Selected Airborne Chemicals, Volume 4.
Subcommittee on Acute Exposure Guideline Levels, Committee on Toxicology Board on Environmental Studies and Toxicology, The National Academy Press, Washington DC, 2004

Estimated Based on Hydrolysis to HF

As noted in B-7 Conclusion. If no reliable LC₅₀ or LCLO 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;

When no studies are available the hydrolysis reaction in air has proven to be reliable based on a 2006 Dow Corning Inc study that demonstrated that Chlorosilane (Monochlorosilane, Dichlorosilane, Trichlorosilane) toxicity can be predicted based on HCl equivalency



Jean, P. A., Gallavan, R. H., Kolesar, G. B., Siddiqui, W. B., Oxley, J. A. and Meeks, R. G. "Chlorosilane Acute Inhalation Toxicity and Development of an LC50 Prediction Model" Inhalation Toxicology, 18:515–522, 2006



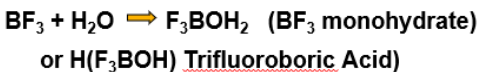
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The values for Phosphorus Pentafluoride, Phosphorus Trifluoride and Tungsten Hexafluoride were estimated based on this principle in the 1995 edition of ISO 10298. They have been changed as a result of the HF value increasing from 966 ppm to 1,307 ppm.

Boron Trifluoride

Most assume that Boron Trifluoride will hydrolyze in air to form HF. It doesn't



In Excess Water



If any Hydrogen Fluoride is formed it is quickly reacted



Jones, W. Ransom, "*Incorrect Assumption of Boron Trifluoride Hydrolyzation to Hydrogen Fluoride and The Effect on Existing Monitoring Techniques*", SSA Journal, Vol. 12, pp 19-23

I'm not sure why Dr. Carol Maslansky selected the Vernot value of 387 ppm since the Rusch 1986 study was also included in the 1992 review. It met all the test criteria, 5 male and 5 female rats. Dr. Sylvie Tissot and Carrie Hamilton reviewed both studies and concluded the Rusch study was more valid with a value of 873 ppm.

I hope that this information is of value to the Working Group. I would be happy to answer any questions regarding these. Unfortunately, I will not be available for the virtual meeting due to international travel.

Sincerely,

Eugene Ngai
President

Name: AMMONIA

Rat LC50: 4230 ppm

C.L.: 4070-4400 ppm

Exposure interval: 1 hour

Obs. interval: 14 days

Animals/test group: 12

Males: 12 Females: 0

Additional data/other species: None

Source: Kapeghian, A.B., Mincer, H.H., Jones, A. B. Verlangieri, A. J. and Waters, I.W. 1982. Acute Inhalation toxicity of ammonia in mice. Bull. Environm. Contam. Toxicol. 29: 371-378.

Methodology conforms to proposed standard?: No

Reason?: Females not used.

Methodology sufficient to accept data as valid?: Yes

1 Hour LC50 (rat):

Normalized?:

1 Hour LC50 (other species): 4230 ppm (mouse)

Normalized?: No

Comments: Delayed deaths observed up to 14 days after exposure, however, most deaths occurred within 72 hours post-exposure. LC50 value close to value determined for mice by Vernot and coworkers (4837 ppm).

Attachment: Fax copy of Kapeghian paper attached.

Reject data due to use of mice which has a lower lung capacity

Name: AMMONIA

Rat LC50: 7338 ppm

C.L.: 6822-7893 ppm

Exposure interval: 1 hour

Obs. interval: None

Animals/test group: 5

Males: 5

Females: 0

Additional data/other species:

1 hour LC50 (mouse): 4837 ppm (C.L. 4409-5305 ppm)

Source: Vernot, E.H., MacEwen, J.D., Haun, C.C., and Kinkead, E.R. 1977. Acute toxicity and skin corrosion data for some organic and inorganic compounds and aqueous solutions. Toxicol. Appl. Pharmacol. 42: 417-423.

Methodology conforms to proposed standard?: No

Reason?: No females used, no observation interval described.

Methodology sufficient to accept data as valid?: No (see comments)

1 Hour LC50 (rat):

Normalized?:

1 Hour LC50 (other species):

Normalized?:

Comments: It is unfortunate that these data are not supported by an observation interval, for I have little doubt that approximately 4000 ppm is a reasonable 1 hour LC50 for rats, based on Union Carbide data and the 1 hour mouse data published by Kapeghian and co-workers. Unfortunately, the absence of an observation interval, especially for a respiratory irritant, is a deficiency that cannot be overlooked.

Attachment: 4 hours at 2000 ppm killed 0/6 rats, 4000 ppm killed 6/6. Chemical Hygiene Fellowship Special Report 10-46, Union Carbide Corp, 1946.

Copy of Vernot paper attached.

Name: AMMONIA

Rat LC50: 16,600 ppm	C.L.: 15,500-17,700 ppm
Exposure interval: 10 - 60 minutes	Obs. interval: 14 days
Animals/test group: 10	Males: 5 Females: 5
Additional data/other species: None	

Source: Appleman, L.M., ten Berge, W.F., and Reuzel, P.G.J. 1982. Acute inhalation toxicity study of ammonia in rats with variable exposure periods. Am. Ind. Hyg. Assoc. J. 43: 662-665.

Methodology conforms to proposed standard?: Yes

Reason?: Used appropriate number of males and females, 1 hour exposure, 14 day observation interval.

Methodology sufficient to accept data as valid?: Yes (see comments)

1 Hour LC50 (rat): 14,070 ppm Normalized?: No

1 Hour LC50 (other species): None Normalized?:

Comments: I still find these data disturbing for several reasons:

1) This is a variable exposure interval study, rather than a true acute inhalation toxicity study designed to determine a 1 hour LC50.

⇒ 2) There is significant variability in response between male and female rats, which cannot be explained by differences in body size or weight alone. For example, at 11,300 ppm, a 60 minute exposure produced 100% mortality in males and 0% in females.

A prudent approach would be to adopt the more conservative male rat data until a 1 hour LC50 assay could be conducted.

Attachment: Male rat LC50: 14,070 ppm, LC100: 16,150 ppm
Female rat LC50: 19,700 ppm, LC100: not determined

Copy of Appleman paper attached.

note all males killed before female level reached.



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Sept 24, 2015

Jack Wert, Technical Manager
Jill Thompson, U.S. TAG Administrator, ISO/TC 58/SC 2
Compressed Gas Association, Inc.
14501 George Carter Way, Suite 103
Chantilly, VA 20151

Subject: A History on the development of CGA P-20 and ISO 10298

It was stated by CGA in ISO TC58 SC2 N1131 Result of systematic review of ISO 10298:2010 "Determination of toxicity of a gas or gas mixture" that

There are inconsistencies between LC₅₀ values in ISO 10298 and CGA P-20 that should be resolved/harmonized (for example, diethyl zinc, chloromethane, hydrogen chloride, triethylaluminum, etc.)

I would like to help resolve this by offering some history as well as the basis for how we derived the latest LC₅₀ values.

History:

I participated on the original CGA Task Force to develop pamphlet P-20 "**Standard for the Classification of Toxic Gas Mixtures**". (Specialty Gas Docket 86-08) This effort was led by Jay Harding of Air Liquide and took over 4 years of continuous effort to develop a table of LC₅₀ values. Besides myself, the only remaining member so this original Task Force is Mike Injaian and Dave Sonneman. We retained the services of Dr. Carol Maslansky, a noted Toxicologist to help us obtain relevant studies and to determine their validity. She also made recommendations for gases that did not have appropriate data and/or adjusted for rat data that was not 1 hour exposures. Jay was also able to locate Vernot who conducted many of the studies for the Air Force in the 1960's and 1970's. He was working for API in 1989 and Jay arranged to meet with him.

In a Dec 1989 meeting Jay presented to ISO Toxicity meeting (US, Canada, UK, France and Germany) the results of the Task Force review. There was agreement that ISO10298 and CGA P-20 define LC₅₀ values as being white albino rats with a 1 hour exposure observed for 14 days in the absence of relevant values would be provisionally assigned by Committee. There was also agreement on the use of a modified Haber calculation to estimate 1 hour LC₅₀ values based on studies with varying exposure times. The attached table 3 Toxic Categories was what was presented to ISO. The table following were the references that were used to develop the LC₅₀ values. These were the basis for the initial P-20T standard in 1990 (Tentative Standard for the Classification of Toxic Gas Mixtures). The table Gas Comparison CGA/ISO summarized the differences in compounds listed between CGA and ISO. Note that diethylzinc and triethylaluminum appears on the ISO list and not on the CGA list.



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After the adoption of P-20T there continued to be information sharing. On March 12, 1992 the CGA Task Force met with Jim Osteen and George Cushmac of DOT to compare data between CGA, DOT and ISO. Dr. Michael Kunde from Germany assisted the ISO Working Group on the review of data. Jay Harding was also an active member of the ISO Working Group in an attempt to harmonize the values. In 1994 P-20 was revised to update some values and to add compounds listed in the proposed ISO standard. ISO 10298 was approved in 1995.

In a Aug 2005 letter I submitted to Specialty Gas and TC58 SC2 WG7 the following information based on more recent testing. I suggested a review and updating of the LC₅₀ values.

- 1. Arsine LC₅₀ of 178 ppm** – The original 20 ppm value was derived from mouse data. Later rat data shows a value of 178 ppm. This is so different than what has been used that this will be left to the reader (US EPA OPPT, Arsine - Proposed Acute Exposure Guideline Levels (AEGs) "Public Draft" Fax-On-Demand item #4922 (IRDC reports))
- 2. Boron Trifluoride LC₅₀ of 873 ppm** – better value from later testing (Rusch, B.M., Hoffman, G.M., McConnell, R.F., and Rinehart, W.E. "Inhalation Toxicity Studies with Boron Trifluoride" Toxicol. Appl. Pharmacol. (1986) Vol. 83, pp 69-78)
- 3. Hydrogen Selenide LC₅₀ of 51 ppm** – original value of 2 ppm was from a guinea pig. (Zwart, A., Arts, J.H.E., Ten Berge, W.F., and Appleman, L.M. "Alternative Acute Inhalation Toxicity Testing by Determination of the Concentration-Time-Mortality Relationship: Experimental Comparison with Standard LC₅₀ Testing," Reg. Tox. and Pharm., Vol. 15, 1992, pp. 278-290)
- 4. Nitric Oxide LC₅₀ of 158 ppm** – assumes that the NO will oxidize to NO₂, (Gray, E., Patton, F.M., Goldberg, S.B. and Kaplan, E., "Toxicity of the Oxides of Nitrogen II. Acute Inhalation Toxicity of Nitrogen Dioxide, Red Fuming Nitric Acid, and White Fuming Nitric Acid," Archives of Industrial Hygiene and Occupational Medicine, (1954) Vol. 10, pp 418-422)
- 5. Silicon Tetrafluoride LC₅₀ of 922 ppm** – original was derived from mouse data (Scheel, L.D., Lane, W.C., Coleman, W.E., "The Toxicity of Polytetrafluoroethylene Pyrolysis Products— Including Carbonyl Fluoride and a Reaction Product, Silicon Tetrafluoride," Am. Ind. Hyg. Assoc. Journal, (1968) Jan-Feb., pp 41-48)

The Specialty Gas Committee elected not to act on this information. TC58 SC2 WG7 however took an active role over the next 3 years to gather more data and to provide a Toxicologist, Dr. Sylvie Tissot, a OECD French National Coordinator to review the data for all of the gases in ISO 10298. Air Products also provided a Toxicologist, Carrie Hamilton to do the same for the CGA. As part of this effort we made every effort to insure that the appropriate studies were referenced and the values defensible.

A key compromise from this effort was the agreement on the LC₅₀ value for HF. This value affected many other fluoride gas LC₅₀ values that were derived based on hydrolysis to HF. (See attached letter)

The Working Group also agreed that 10298 would only focus on compressed gases. Liquids that are used for gas mixtures would be summarized in a separate Appendix (A.2) as informative. There was little effort to try to seek additional data for these. It was also agreed to remove the tables for FTSC since that is now addressed in ISO 14456 Gas properties and associated classification (FTSC) codes. The revised standard was approved on June 12, 2008.



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LC₅₀ Differences

I would like to address some of the questions

1. Chloromethane LC₅₀ was changed from 8,300 ppm to 5,133 was a change by Dr. Tissot based on a more relevant study. (IZMEROV, N.F., et al. Toxicometric Parameters of Industrial Toxic Chemicals Under Single Exposure, Moscow, Centre of International Projects, GKNT, 1982 in IUCLID). There was no reference listed in the 1996 ISO 10298, just a notation that it was time adjusted mouse data. P-20 adopted the value from ISO.
2. My comments Oct 14, 2008 to CGA regarding triethylaluminum (TEAL) and diethyl zinc (DEZ) was incorporated in the CGA comments to TC58 SC2 WG7.

“The organometallic compounds are not acutely toxic. Since they are violently water reactive and pyrophoric, they will react immediately in air to inert compounds like Zinc Oxide and Aluminum Oxide. Assignment of a conservative value of 10 ppm would suggest that they are more toxic than Arsine or Hydrogen Selenide”

This was discussed and ISO 10298 was changed to reflect this opinion. SDS from many DEZ and TEAL manufacturing companies have been reviewed, Akzo Nobel, Dow Electronics, SAFC, none listed toxicity as a hazard. As noted earlier, CGA in the 1994 revision insert these compounds based on the listing in ISO 10298.

3. Hydrogen chloride has been listed as having an LC₅₀ of 3120 ppm since P-20 was developed and was based on a Vernot study in 1977. Based on P-20 ISO adopted the same value in 1995. This was far better than the DOT value of 1175 ppm. Both toxicologist agreed in the 2008 review that the HARTZELL, G.E., PACKHAM, S.C., GRAND, A.F. and SWITZER, W.G. Modeling of toxicological effects of fire gases: III. Quantification of post-exposure lethality of rats from exposure to HCl. J Fire Sci, 3, 1985, pp. 195-207 was a more accurate study. This concluded a value of 2810 ppm. I cannot remember the reasons for this determination. As noted by Jay Harding in the comparison of DOT and CGA values, a variance of 25% in values between studies is not significant to a toxicologist. Especially when using earlier studies that were not as well controlled. This difference is 10%.

In closing, considerable effort was put into the revision of ISO 10298 by CGA and EIGA member companies. If more recent test reports are found or if these is still a conflict, every effort should be made to have it reviewed by a Toxicologist to validate the values as was done originally for P-20 and for the revised ISO 10298 standard. I am available to discuss this further.

Regards

Eugene Ngai

Enclosures

Attachment 1, Ngai to CGA, History of CGA P-20 and ISO 10298

T A B L E 3

T O X I C C A T E G O R I E S

PRODUCT	TOXICITY LEVEL PPM	ADJUSTED VALUE	ISO DESCRIPTION	[200 ppm] CATEGORY A		[5000 ppm] CATEGORY D		200 ppm using ISO		5000 ppm using ISO	
				> or = %	> or = %	> or = %	> or = %	using ISO	using ISO	using ISO	using ISO
AMMONIA	14070		LC50 RAT	N/A	N/A	N/A	N/A	0.0	0.0	0.0	0.0
ARSLINE	26	20	LC50 MUS time adj.	13.000	0.520	0.520	10.0	0.0	0.4	0.0	0.4
BORON TRICHLORIDE	2541		LC50 RAT	N/A	50.820	50.820	0.0	0.0	0.0	0.0	0.0
BORON TRIFLUORIDE	806	800	LC50 RAT time adj.	N/A	16.120	16.120	N/A	N/A	16.0	0.0	16.0
BROMINE CHLORIDE	2860		Est. from HBr	N/A	57.200	57.200	0.0	0.0	0.0	0.0	0.0
CARBON MONOXIDE	3760		LC50 RAT time adj.	N/A	75.200	75.200	0.0	0.0	0.0	0.0	0.0
CARBONYL FLUORIDE	360		LC50 RAT	N/A	7.200	7.200	0.0	0.0	0.0	0.0	0.0
CARBONYL SULFIDE	712	900	Est. from H2S	N/A	14.240	14.240	N/A	N/A	18.0	0.0	18.0
CHLORINE	293		LC50 RAT	N/A	5.860	5.860	0.0	0.0	0.0	0.0	0.0
CHLORINE PENTAFLUORIDE	122		LC50 RAT	61.000	2.440	2.440	0.0	0.0	0.0	0.0	0.0
CHLORINE TRIFLUORIDE	299		LC50 RAT	N/A	5.980	5.980	0.0	0.0	0.0	0.0	0.0
CYANOGEN	350		LC50 RAT	N/A	7.000	7.000	0.0	0.0	0.0	0.0	0.0
CYANOGEN CHLORIDE	118	80	LC50 RAT time adj.	59.000	2.360	2.360	40.0	40.0	1.6	1.6	1.6
DIBORANE	160	80	LC50 RAT time adj.	80.000	3.200	3.200	40.0	40.0	1.6	1.6	1.6
DICHLOROSILANE	314		LC50 RAT	N/A	6.280	6.280	0.0	0.0	0.0	0.0	0.0
DIETHYLAMINE	8000		LC50 RAT time adj.	N/A	N/A	N/A	0.0	0.0	0.0	0.0	0.0
DIMETHYLAMINE	13620	11000	LC50 RAT time adj.	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
ETHYLAMINE	16000		LC50 RAT time adj.	N/A	N/A	N/A	N/A	N/A	0.0	0.0	0.0
ETHYLENE OXIDE	2920	2900	LC50 RAT time adj.	N/A	58.400	58.400	N/A	N/A	58.0	58.0	58.0
ETHYL FLUORIDE	>26%		LC50 RAT	DELETED	DELETED	DELETED	DELETED	DELETED	DELETED	DELETED	DELETED
FLUORINE	185		LC50 RAT	92.500	3.700	3.700	0.0	0.0	0.0	0.0	0.0
GERMANE	26	20	Est. from Ash3	13.000	0.520	0.520	10.0	10.0	0.4	0.4	0.4
HEXAFLUOROACETONE	481	470	LC50 RAT time adj.	N/A	9.620	9.620	N/A	N/A	9.4	9.4	9.4
HYDROGEN BROMIDE	2860		LC50 RAT	N/A	57.200	57.200	0.0	0.0	0.0	0.0	0.0
HYDROGEN CHLORIDE	3120		LC50 RAT	N/A	62.400	62.400	0.0	0.0	0.0	0.0	0.0
HYDROGEN FLUORIDE	1276		LC50 RAT	N/A	25.520	25.520	0.0	0.0	0.0	0.0	0.0
HYDROGEN IODIDE	2860		LC50 RAT	N/A	57.200	57.200	0.0	0.0	0.0	0.0	0.0
HYDROGEN SELENIDE	2.8	2	Est. from HBr	N/A	1.400	1.400	0.0	1.0	0.0	0.0	0.0
HYDROGEN SULFIDE	712		LC50 GPg	N/A	14.240	14.240	0.0	0.0	0.0	0.0	0.0
METHYLAMINE	7000		LC50 MUS	N/A	N/A	N/A	N/A	0.0	0.0	0.0	0.0
METHYL BROMIDE	1164	850	LC50 MUS	N/A	23.280	23.280	N/A	N/A	17.0	17.0	17.0
METHYL CHLORIDE	>7%	8300	LC50 UNK time adj.	DELETED	DELETED	DELETED	DELETED	DELETED	DELETED	DELETED	DELETED
METHYL CHLOROSILANE	1200		Est. twice Dichlor	N/A	12.000	12.000	0.0	0.0	0.0	0.0	0.0
METHYL DICHLOROSILANE	600		LC50 RAT time adj.	N/A	27.000	27.000	0.0	0.0	0.0	0.0	0.0
METHYL MERCAPTAN	1350		LC50 RAT time adj.	N/A	57.500	57.500	0.0	0.0	0.0	0.0	0.0
NITRIC OXIDE (+some N2O4)	115		LC50 RAT for NO2	57.500	2.300	2.300	0.0	0.0	0.0	0.0	0.0
NITROGEN DIOXIDE	115		LC50 RAT	57.500	2.300	2.300	0.0	0.0	0.0	0.0	0.0
NITROGEN TRIFLUORIDE	6700		LC50 RAT	N/A	N/A	N/A	0.0	0.0	0.0	0.0	0.0
NITROGEN TRIOXIDE	57		calc. N2O3=NO+NO2	28.500	1.140	1.140	0.0	0.0	0.0	0.0	0.0
NITROSYL CHLORIDE	115		Est. from NO2	57.500	2.300	2.300	0.0	0.0	0.0	0.0	0.0
OXYGEN DIFLUORIDE	2.6		LC50 RAT	1.300	0.052	0.052	0.0	0.0	0.0	0.0	0.0
PERCHLORYL FLUORIDE	770		LC50 RAT time adj.	N/A	15.400	15.400	0.0	0.0	0.0	0.0	0.0
PHOSGENE	5		LC50 RAT time adj.	2.500	0.100	0.100	0.0	0.0	0.0	0.0	0.0
PHOSPHINE	22	20	LC50 RAT time adj.	11.000	0.440	0.440	10.0	10.0	0.4	0.4	0.4
PHOSPHOROUS PENTAFLUORIDE	255	250	Est. 1/5 of HF	N/A	5.104	5.104	N/A	N/A	5.0	5.0	5.0
SELENIUM HEXAFLUORIDE	50		LC50 RAT adj.	25.000	1.000	1.000	0.0	0.0	0.0	0.0	0.0
SILICON TETRAFLUORIDE	319		LC50 RAT for HF/4	N/A	6.380	6.380	0.0	0.0	0.0	0.0	0.0
STIBINE	40	90	IDLH	20.000	0.800	0.800	45.0	45.0	1.8	1.8	1.8
SULFUR DIOXIDE	2520		LC50 RAT	N/A	50.400	50.400	0.0	0.0	0.0	0.0	0.0
SULFUR TETRAFLUORIDE	319		LC50 RAT for HF/4	N/A	6.380	6.380	0.0	0.0	0.0	0.0	0.0
SULFURYL FLUORIDE	3020		LC50 RAT	N/A	60.400	60.400	0.0	0.0	0.0	0.0	0.0
TELLURIUM HEXAFLUORIDE	25		LC50 RAT adj.	12.500	0.500	0.500	0.0	0.0	0.0	0.0	0.0
TRIFLUOROACETYLCHLORIDE	12		Est. as Trichloro.	6.000	0.240	0.240	0.0	0.0	0.0	0.0	0.0
TUNGSTEN HEXAFLUORIDE	1276		Est. from HF	N/A	25.520	25.520	0.0	0.0	0.0	0.0	0.0

NOTE: COS data is LCLO MUS time adj.; CH3Br is LC50 RAT time adj.; CH3Cl is LC50MUS time adj.; Sbh3 is LCLO GPg.

TOXIDOC5.WK1

1/2/90

this includes latest ISO data

No.	SYMBOL	TOXICITY LEVEL PPM	DESCRIPTION	DOCUMENTATION	
01	NH3 -----	14070	LC50 RAT	Appleman, L. M., et al, 1982. Male rat only, more conservative.	****
02	Ash3	20 *	LC50 MUS time adj.	Levy, 1947, from National Research Council, 1984. Should be ~26 ppm.	
03	BC13	2541	LC50 RAT	Vernot, E.H., et al, 1977. Males only, more susceptible.	
04	BF3	800 *	LC50 RAT time adj.	Rusch, G.M., et al, 1986. 403 ppm for 4 hours.	
05	BrCl -----	2860	Est. from HBr	Estimated, based on HBr data from Vernot et al, 1977.	
06	CO	3760	LC50 RAT time adj.	Rose, C.S., et al, 1970. 1880 ppm for 4 hours.	
07	COF2	360	LC50 RAT	Scheel, L.D., et al, 1968.	
08	COS	900 *	LCL0 MUS time adj.	Berichte der Deutschen Chemischen Gesellschaft. 76,299,43. 1200ppm/35M	
09	C12 -----	293	LC50 RAT	Vernot, E.H., et al, 1977. No females, no observation time.	
10	C1F5	122	LC50 RAT	Darmer, K.I., et al, 1972. (no females used).	
11	C1F3	299	LC50 RAT	Darmer, K.I., et al, 1972. (no females used).	
12	C2N2	350	LC50 RAT	McNerney, J.M., and Schrenk, H.H., 1960. Calculated from graph.	
13	CNC12	80 *	LC50 RAT time adj.	THICSM, ITI, Tokyo, 1977. 118 ppm for 30 minutes; unknown number, observation time.	
14	B2H6 -----	80 *	LC50 RAT time adj.	Adams, R.M., 1964. 40 ppm for 4 hours.	
15	SiH2C12	314	LC50 RAT	Chemical Hygiene Fellowship Report 49-112, UCC, 1986.	
16	(C2H5)2NH	8000	LC50 RAT time adj.	Smyth, H.F., et al, 1954. 4000 ppm for 4 hours on 6 rats, sex unknown.	
17	(CH3)2NH	11000 *	LC50 RAT time adj.	Steinhagen, W.H., et al, 1982. 4540 ppm for 6 hours; unknown number observed 2 days.	****
18	C2H5NH2	16000	LC50 RAT time adj.	Smyth, H.F., et al, 1954. 8000 ppm killed 2/6 in 4 hours.	
19	C2H4O ----	2900 *	LC50 RAT time adj.	Jacobson, K. H., et al, 1956. 1460 ppm for 4 hours; no females.	
20	C2H5F	>26%	LC50 RAT time adj.	Chemical Hygiene Fellowship Report 10-28, UCC, 1947.	
21	F2	185	LC50 RAT	Keplinger, M.L. and Suissa, L.W., 1968. 10 rats, sex unknown, 14 days.	****
22	GeH4	20 *	Est. from AsH3	Levy, 1947, from National Research Council, 1984. Should be ~26 ppm.	
23	C3OF6	470 *	LC50 RAT time adj.	Borzella, J.F. and Lester, D., 1964. Number, sex, observation time unknown.	
24	HBr -----	2860	LC50 RAT	Vernot, E.H., et al, 1977. No females, no observation time.	
25	HCl	3120	LC50 RAT	Vernot, E.H., et al, 1977. No females or observation; more conservative than Darmer.	
26	HF	1276	LC50 RAT	Darmer, K.I. et al, 1972. No females. Confirmed by Rosenholtz (1307 ppm).	
27	HI	2860	Est. from HBr	Estimated, based on HBr data from Vernot et al, 1977.	
28	H2Se	2 *	LC50 GPG	Dudley, H.C. and Miller, J.W., 1941.	
29	H2S -----	712	LC50 RAT	Vernot, E.H., et al, 1977. No females or observation.	
30	CH3NH2	7000	LC50 MUS	Mezentseva, N.V., 1956.	
31	CH3Br	850 *	LC50 RAT time adj.	Toxicology and Applied Pharmacology. 81,183,85. 302 ppm for 8 hours.	
32	CH3Cl	8300 *	LC50 MUS time adj.	National Institutes of Health, Bulletin 191,1,49. 3146 ppm for 7 hours.	****
33	SiClH2CH3	1200	Est. twice No. 34	Estimated, based on Marhold, J.V., 1972.	
34	SiCl2HCH3	600	LC50 RAT time adj.	Marhold, J.V., 1972. [Czechoslovakia]	
35	CH3SH	1350	LC50 RAT time adj.	Tansy, M.F., et al, 1981. 675 ppm for 4 hours.	
36	NO	115	LC50 RAT for NO2	Estimated, based on NO2 data from Carson, R.T. et al, 1962.	
37	NO2	115	LC50 RAT	Carson, R.T. et al, 1962. No females.	
38	NF3	6700	LC50 RAT	Vernot, E.H. et al, 1973. No females.	****
39	N2O3 ----	57	calc. N2O3=NO+NO2	Estimated, based on NO2 data from Carson, R.T. et al, 1962.	
40	NOC1	115	Est. from NO2	Estimated, based on NO2 data from Carson, R.T. et al, 1962.	
41	OF2	2.6	LC50 RAT	Darmer, K.I. et al, 1972. No females.	
42	C1FO3	770	LC50 RAT time adj.	THICSM, ITI, Tokyo, 1977. 385 ppm for 4 hours; unknown number, sex, observation.	
43	COC12	5	LC50 RAT time adj.	Based on 4 ppm/75 min [Rinehart and Hatch, 1964] and 12 ppm/30 min [Chasis, 1944].	
44	PH3 -----	20 *	LC50 RAT time adj.	Waritz, R.S. and Brown, R.M., 1975. 11 ppm for 4 hours; no females; unclear observ.	
45	PF5	250 *	Est. 1/5 of HF	Estimated, based on HF data from Darmer, K.I. et al, 1972.	
46	SeF6	50	LC50 RAT adj.	Kimmerle, G., 1959.	
47	SiF4	319	LC50 RAT for HF/4	Estimated, based on HF data from Darmer, K.I. et al, 1972.	
48	SbH3	90 *	LCL0 GPG	Browning, E. Toxicology of Industrial Metals. London: Butterworths, 1961.	
49	SO2 -----	2520	LC50 RAT	NTIS publication AD-A148-952; still searching for document.	
50	SF4	319	LC50 RAT for HF/4	Estimated, based on HF data from Darmer, K.I. et al, 1972.	
51	SO2F2	3020	LC50 RAT	Vernot, E.H., et al, 1977. No observation; conservative female data used.	
52	TeF6	25	LC50 RAT adj.	Kimmerle, G., 1959.	****
53	C2F3OC1	12	Est. as Trichloro..	Estimated, based on trichloroacetylchloride, RTECS.	
54	WF6 -----	1276	Est. from HF	Estimated, based on HF data from Darmer, K.I. et al, 1972.	

Gas Comparison CGA/ISO

GASES ON BOTH LISTS	CGA ONLY	ISO ONLY
AMMONIA	BROMINE CHLORIDE	ANTIMONY PENTAFLUORIDE
BORON TRICHLORIDE	CARBONYL FLUORIDE	BIS-TRIFLUOROMETHYL PEROXIDE
BORON TRIFLUORIDE	DIETHYLAMINE	BROMINE PENTAFLUORIDE
CARBON MONOXIDE	METHYL CHLOROSILANE	BROMINE TRIFLUORIDE
CARBONYL FLUORIDE	METHYL DICHLOROSILANE	BROMOACETONE
CHLORINE SULFIDE	NITROGEN TRIFLUORIDE	1,3-BUTADIENE(INHIBITED)
CHLORINE	PERCHLORYL FLUORIDE	COAL GAS
CHLORINE PENTAFLUORIDE	SELENIUM HEXAFLUORIDE	CYCLOPROPANE
CYANOGEN	TELLURIUM HEXAFLUORIDE	DEUTERIUM CHLORIDE
CYANOGEN CHLORIDE	TRIFLUOROACETYLCHLORIDE	DEUTERIUM FLUORIDE
DIBORANE		DEUTERIUM SELENIDE
DICHLOROSILANE		DEUTERIUM SULFIDE
DIMETHYLAMINE		DIBROMODIFLUOROMETHANE
ETHYLAMINE		DICHLORO-2-CHLOROVINYL-ARSINE
ETHYLENE OXIDE		DIETHYLZINC
FLUORINE		DIMETHYLSILANE
GERMANE		DIPHOSGENE
HEXAFLUOROACETONE		ETHYLDICHLOROARSINE
HYDROGEN BROMIDE		HEPTAFLUOROBUTYRONITRILE
HYDROGEN CHLORIDE		HEXAFLUOROCYCLOBUTENE
HYDROGEN FLUORIDE		HYDROGEN CYANIDE
HYDROGEN IODIDE		IODINE PENTAFLUORIDE
HYDROGEN SELENIDE		IODOTRIFLUOROMETHANE
HYDROGEN SULFIDE		METHYLDICHLOROARSINE
METHYLAMINE		METHYL VINYL ETHER (INHIBITED)
METHYL BROMIDE		MUSTARD GAS
METHYL CHLORIDE		NICKEL CARBONYL
METHYL MERCAPTAN		OZONE
NITRIC OXIDE (+SOME N2O4)		PENTAFLUOROPROPIONITRILE
NITROGEN DIOXIDE		PERFLUORO-2-BUTENE
NITROGEN TRIOXIDE		PENTABORANE
NITROSYL CHLORIDE		PHENYL CARBYLAMINE CHLORIDE
OXYGEN DIFLUORIDE		PHOSPHORUS TRIFLUORIDE
PHOSGENE		PROPYLENE OXIDE
PHOSPHINE		SILANE
PHOSPHOROUS PENTAFLUORIDE		SILICON TETRACHLORIDE
SILICON TETRAFLUORIDE		TETRAETHYL LEAD
STIBINE		TETRAFLUOROHYDRAZINE
SULFUR DIOXIDE		TETRAMETHYL LEAD
SULFUR TETRAFLUORIDE		TRIETHYL ALUMINUM
STIBINE		TRIETHYL BORANE
SULFUR DIOXIDE		TRIFLUOROACETONITRILE
SULFUR TETRAFLUORIDE		TRIFLUOROETHYLENE
SULFURYL FLUORIDE		TRIETHYLAMINE
TUNGSTEN HEXAFLUORIDE		TRIMETHYLSILANE
		TRIMETHYLSTIBINE
		URANIUM HEXAFLUORIDE
		VINYL BROMIDE (INHIBITED)
		VINYL CHLORIDE (INHIBITED)
		VINYL FLUORIDE (INHIBITED)


Air Products and Chemicals, Inc.

7201 Hamilton Boulevard
 Allentown, PA 18195-1501
 Telephone (610) 706-2269
 Fax (610) 706-7029
 ngaiey@airproducts.com

Dr. Sylvie Tissot
 OECD French National Coordinator
 Toxicological Expertise Unit
 INERIS
 Parc Technologique Alata
 2 F-60550 Verneuil-en-Halatte

Subject: LC50 Value for ISO 10298

Dear Dr. Tissot,

Since the ISO10298 committee meeting of January 15, 2008, Air Products and Chemicals, Inc. has undertaken a review of the studies related to hydrogen fluoride acute inhalation exposures. We believe that the 966 ppm LC₅₀ value for hydrogen fluoride, which is currently included in ISO10298, is not the most appropriate value to use.

Table 3-4 of the 2004 US National Advisory Committee AEGL review for Hydrogen Fluoride¹ lists the relevant 1-hour rat studies as follows:

<u>Concentration (ppm)</u>	<u>Effect</u>	<u>Reference</u>
2,300	LC ₅₀	Haskell Laboratory 1990
2,039	LC ₁₀	Dalbey et al. 1998
1,395	LC ₅₀	Wohlslagel et al. 1976
1,307	LC ₅₀	Rosenholz et al. 1963
1,276	LC ₅₀	MacEwen and Vernot 1970
966	LC ₅₀	Vernot et al. 1977

As agreed to in the ISO 10298 committee, 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 the 1995 ISO10298 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 wholebody 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 minimises 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. However, the test performer has the option of using other systems (e.g., whole-body inhalation chambers) when justification can be made.^{2,3}

- 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 overestimated 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.¹

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

Based on these technical points, the most appropriate value for hydrogen fluoride is the Haskell (1990) LC₅₀ value of 2,300 ppm. This is also supported by the Dalbey et al. (1998) work showing the LC₅₀ to be >2,039 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:

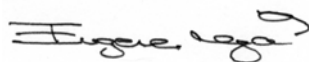
Similar 60-min LC₅₀ values for the rat were found by Wohlschlager et al. (1976), Rosenholtz et al. (1963), and MacEwen and Vernot (1970); 1,395, 1,307, and 1,276 ppm, respectively.¹

The mean of the five LC₅₀ values is 1,449 ppm, and the median LC₅₀ value is 1,307 ppm. The median LC₅₀ of 1,307 ppm could be adopted for hydrogen fluoride as a reasonable value.

Based on the above information, we propose adopting the median 1-hour rat LC₅₀ value of 1,307 ppm. As noted at the meeting of January 15, 2008 in Paris, the value that is adopted for hydrogen fluoride will have a significant impact on the classification of the other hydrolyzable fluoride gases such as phosphorus trifluoride and tungsten hexafluoride. Tungsten hexafluoride has an estimated LC₅₀ value of 160 ppm based on a 966 ppm 1-hour LC₅₀ for hydrogen fluoride. This value would result in the classification of tungsten hexafluoride as a highly toxic gas, and severely restrict packaging and transportation options. If the 1,307 ppm 1-hour LC₅₀ is adopted, tungsten hexafluoride would have an estimated LC₅₀ value of 218 ppm which would cause tungsten hexafluoride to be classified as toxic rather than highly toxic. This approach would also make it easier to harmonize ISO10298 with CGA P-20.

We would be happy to discuss this with you further by telephone. We are anxious to reach agreement on this for the final draft of ISO10298, which is due January 25, 2008.

Sincerely,



Eugene Y. Ngai
Director of ER & Disposal Technology



Carrie E. Hamilton
Product Safety Specialist - Toxicology

cc: Hervé Barthélémy
Nicole Legent

References

1. "Acute Exposure Guideline Levels for Selected Airborne Chemicals, Volume 4", Subcommittee on Acute Exposure Guideline Levels, Committee on Toxicology Board on Environmental Studies and Toxicology, The National Academy Press, Washington DC, 2004
2. "OECD Guideline for the Testing of Chemicals", Draft Proposal for New Guideline: #433 (2004)
3. "OECD Guideline for the Testing of Chemicals", Draft Proposal for New Guideline: #436 (2005)



Chemically Speaking LLC

26 Casper Berger Road
Whitehouse Station, NJ 08889
www.chemicallyspeakingllc.com

Jan 17, 2013

To: ISO/TC 58/SC 2/WG 7
Jack Wert-CGA

Re: ISO/NP 14456 "Gas properties and associated classification (FTSC) codes"

As noted, the FTSC should be updated with the data from ISO 10298. Changes to ISO 10298 were noted in my letter dated Oct 18, 2011 "New standard on "Gas properties". Please note the following edits

Table 5: Tungsten Hexafluoride T changed from 3 to 2 based on item 3 of my letter

A key revision was establishment of the LC₅₀ for hydrogen fluoride at 1307 ppm which was the value from the most technically sound study. (E. Ngai & C. Hamilton letter "LC₅₀ Value for ISO 10298" to Dr. S Tissot, dated Jan 24, 2008) "The more recent hydrogen fluoride studies, which were not publicly available when the 1995 ISO10298 was adopted, are technically better than the older studies The mean of the five LC₅₀ values is 1,449 ppm, and the median LC₅₀ value is 1,307 ppm. This revision affected the values estimated for the hydrolyzable fluoride gases such as tungsten hexafluoride which do not have actual toxic studies.

Table 8: Germane T changed from 3 to 2 based on updated study

Table 9: Dimethylzinc and Trimethylaluminum T changed from 3 to 1 based on Item 7 of my letter

Table A.2 lists the metal alkyls such diethylzinc as having an LC₅₀ of 10 ppm which would suggest that they are more toxic than phosphine and arsine. There is no data to support this. In transportation they are classified as pyrophoric water reactive liquids not toxic.

Should there be any questions, please contact me

Eugene Ngai