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COMMITTEE OF EXPERTS ON THE TRANSPORT OF DANGEROUS GOODS AND ON THE GLOBALLY HARMONIZED SYSTEM OF CLASSIFICATION AND LABELLING OF CHEMICALS
Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals
(Sixth session, 10-12 December 2003, agenda item 2)

PROSOSALS OF AMENDMENTS TO THE GLOBALLY HARMONIZED SYSTEM OF CLASSIFICATION AND LABELLING OF CHEMICALS (GHS)

Classification of gas mixtures for toxic effects

Transmitted by the European Industrial Gases Association (EIGA)

Introduction

At the 5th session of the Sub-Committee, EIGA presented a paper about the classification of gas mixtures for their toxic effects (document ST/SG/AC.10/C.4/2003/1 dated 21 March 2003) which proposed changes to para. 3.1.3.6 of document ST/SG/AC.10/30. Several member states found it difficult to measure the real extent of the problem and EIGA was prompted to further build the case and give more evidence of the problem and a better insight why the additivity formula does not provide appropriate classification results (see report of the 5th session, ST/SG/AC.10/C.4/10, paras. 31 to 34). EIGA therefore is providing the background for this proposal.

Background

A large number of speciality gas mixtures are produced by the gas industry for use in a wide range of applications, including semiconductor manufacture, medical and healthcare, automotive testing, environmental monitoring and university R & D, etc. Many of these mixtures are specifically produced for particular customer use or at least in low production volumes. Thousands of exclusive mixtures are made on demand. The range of mixtures is infinite and can contain up to 20 different gases in variable concentrations.

For such preparations, there is no human experience of their toxic effects as a mixture and a calculation method needed to be developed for a proper classification. Also, using the GHS provisions of Note (e)(ii) to Table 3.1.1 (ST/SG/AC.10/30) is not a viable option for such one-off gas mixtures because it would allow experts to come with different classifications.

It is desirable that the overall toxicity of the gas mixture is determined by means of calculation based on the measured toxicity of individual components. This approach ensures that a consistent and unequivocal classification of the mixtures will be implemented by the gas industry. The GHS came to the same conclusion in Figure 3.1.1 referring then to the additivity formula of 3.1.3.6.1. This formula is unacceptable to EIGA for workshop use. EIGA proposes an alternative calculation formula that has been in use for many years and provides acceptable results.

The issue

Under its para. **3.1.3.6**, the GHS allows a general additivity formula to be used for mixtures. It details principles to enable the classification of mixtures for acute toxic effects in respect of oral, dermal or inhalation toxicity. It allows the transition from pure products to mixtures and provides a formula that allows the calculation of the Acute Toxicity Estimate (ATE) when data are available for all ingredients. The following formula has been adopted under 3.1.3.6.1:

> *"The ATE of the mixture is determined by calculation from the ATE values for all relevant ingredients according to the following formula below for Oral, Dermal or Inhalation Toxicity:*
>
> $$\frac{100}{\text{ATEmix}} = \sum_{n} \frac{\text{Ci}}{\text{ATEi}}$$
>
> *where:*
>
> C_i = *concentration of ingredient i*
> *n ingredients and i is running from 1 to n*
> ATE_i = *Acute Toxicity Estimate of ingredient i."*

This formula is a derivative of the one that has been in use for many years in the transport regulations but is totally unfit for work place conditions. When applied to gases, the formula gives anomalous and a substantial understatement of the hazard. This leads to potentially dangerous results that could lead to personal injury or harm.

To illustrate the dangers of adopting this method of calculation Table 1 below gives ATE values for three common gases; ammonia, carbon monoxide and hydrogen chloride when mixed with non toxic gases (GHS Value %). For appreciation of the gross discrepancy, various accepted occupational exposure limits in **ppmV** have been added.

The following abbreviations are used:

- TWA: Time-Weighted Average concentration for a normal 8-hour workday and a 40-hour workweek, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect.

- STEL : Short term exposure limit is defined as a 15- minute TWA exposure which should not be exceeded at any time during a workday.

- IDLH: Immediately Dangerous to Life and Health, concentration from which a worker could escape without any escape-impairing symptoms or any irreversible health effects.

Comparison between existing OEL values and GHS cut-off values

PRODUCT	VOLUME % IN MIXTURES	GHS TOXICITY CATEGORY
AMMONIA TWA 20 ppmV STEL 35 ppmV IDLH 500 ppmV	Between 100 and 80% Between 80 and 40% Less than 40%	Category 3 Category 4 Category 5 or Non toxic
HYDROGEN CHLORIDE TWA 5 ppmV STEL 5 ppmV IDLH 100ppmV	Between 100 and 56.2% Between 56.2 and 28.1% Less than 28.1%	Category 3 Category 4 Category 5 or Non toxic
CARBON MONOXIDE TWA 25 ppmV STEL 400 ppmV IDLH 1500 ppmV	Between 100 and 75.2% Between 75.2 and 37.6% Less than 37.6%	Category 3 Category 4 Category 5 or Non toxic

It is quite obvious that a potential release of 376.000 ppmV of Carbon Monoxide, 250 times higher than the IDLH, cannot be considered as harmless. There is also a flagrant imbalance in the approach taken between acute toxicity and e.g. reproductive toxicity. Carbon monoxide is a reproductive toxicant of category 1 and an eventual mixture with other inert gases remains in that category above 0.1% of carbon monoxide concentration.
EIGA considers this approach totally unsafe and strongly recommends not using the formula for gases.

Proposal

EIGA proposes to retain the four categories as applicable to gases and base the categories on the approach adopted in the GHS for the other health hazards (Carcinogenic, mutagenic and reproductive toxicity) and on the basis of modified EU (4 categories rather than 3), which has proved to work effectively and gives intuitively acceptable results.

EIGA Proposal for cut-off values for gas mixtures

Gas classified	Concentration limits triggering classification of the mixture as			
	Category 1 *100 ppmV	**Category 2** *500ppmV	**Category 3** *2500ppmV	**Category 4** *5000ppmV
Category 1	More than 1%	1.0-0.5%	0.5-0.2%	0.2-0.02%
Category 2		More than 2.0%	2.0-1.0%	1.0-0.2%
Category 3			More than 5%	5-0.5%
Category 4				More than 5%

* LC_{50}- 4 Hours.

For example under the existing GHS system the cut-off value for a carbon monoxide mixture moving from the harmful to the toxic classification is 75.2 Vol % of CO whereas the cut off value in these EIGA proposals would be 5 Vol %. If these concentrations are compared with the IDLH (Immediately dangerous to life or health value) of 1500 ppmV (0.15 Vol %) and the STEL (Short term exposure level) of 400 ppmV (0.04 Vol %) it is apparent that the method of calculation in the EIGA proposal is more applicable and safer than the existing ATE formula.

Appendices

Several delegates have expressed an interest in what substances are actually involved. EIGA therefore has annexed a table to this paper. The table lists 55 gases in descending order of toxicity as expressed by their LC50 both in UN values (1 hour) and GHS values (4 hours). The table then lists the cut-off values for mixtures with non toxic gases for both the GHS additivity formula and the EIGA proposal. For additional appreciation, currently used values in the EU have been listed.
As an example:

Using the GHS additivity formula, UN 1045 Fluorine with an LC50 of 92.5 ppmV would only remain in Category 1 if its concentration is over 92.5%. Between 18.5 and 92.5% it would move to category 2, between 3.7 and 18.5% to category 3 and between 3.7 and 1.85% to category 4. Conversely, the EIGA values would be 1, 0.5, 0.2 and 0.02% and the EU values 1, 0.2 and 0.02 (the EU only considers three levels).

UN Nos	Name	LC_{50} 1 h (UN)	LC_{50} 4h (GHS)	CONCENTRATION LIMIT % **category 1**		CONCENTRATION LIMIT % **category 2**		CONCENTRATION LIMIT % **category 3**		CONCENTRATION LIMIT % **category 3**		Non toxic		EU CLASSIFICATION			UN	UN
				GHS	EIGA proposal	GHS	EIGA proposal	GHS	EIGA proposal	GHS	EIGA proposal	GHS	EIGA proposal	Very toxic%	Toxic %	Harmful %	Class.	Subs. Risks
2202	Hydrogen selenide	2	1	> **1**	**> 1**	**0.2 - 1**	**0.5 - 1**	**0.04 - 0.2**	**0.2 - 0.5**	**0.02 - 0.04**	**0.02 - 0.2**	**< 0.02**	**< 0.02**	> 1	1 - 0.2	0.2 - 0.02	2.3	2.1
3160	Hydrogen telluride LC50 from ISO10298	2	1	> **1**	**> 1**	**0.2 - 1**	**0.5 - 1**	**0.04 - 0.2**	**0.2 - 0.5**	**0.02 - 0.04**	**0.02 - 0.2**	**< 0.02**	**< 0.02**	> 1	1 - 0.2	0.2 - 0.02	2.3	2.1
1076	Phosgene	5	2.5	> **2.5**	**> 1**	**0.5 - 2.5**	**0.5 - 1**	**0.1 - 0.5**	**0.2 - 0.5**	**0.05 - 0.1**	**0.02 - 0.2**	**< 0.05**	**< 0.02**	> 1	1 - 0.2	0.2 - 0.02	2.3	8
3308	Arsenic pentafluoride LC50 FROM ISO 10298	20	10	> **10**	**> 1**	**2 - 10**	**0.5 - 1**	**0.4 - 2**	**0.2 - 0.5**	**0.2 - 0.4**	**0.02 - 0.2**	**< 0.2**	**< 0.02**		> 0.2	0.2 - 0.1	2.3	8
2188	Arsine	20	10	> **10**	**> 1**	**2 - 10**	**0.5 - 1**	**0.4 - 2**	**0.2 - 0.5**	**0.2 - 0.4**	**0.02 - 0.2**	**< 0.2**	**< 0.02**	> 1	1 - 0.2	0.2 - 0.02	2.3	2.1
2199	Phosphine	20	10	> **10**	**> 1**	**2 - 10**	**0.5 - 1**	**0.4 - 2**	**0.2 - 0.5**	**0.2 - 0.4**	**0.02 - 0.2**	**< 0.2**	**< 0.02**	> 1	1 - 0.2	0.2 - 0.02	2.3	2.1
2676	Stibine	20	10	> **10**	**> 1**	**2 - 10**	**0.5 - 1**	**0.4 - 2**	**0.2 - 0.5**	**0.2 - 0.4**	**0.02 - 0.2**	**< 0.2**	**< 0.02**	> 1	1 - 0.2	0.2 - 0.02	2.3	2.1
1069	Nitrosyl chloride	35	17.5	> **17.5**	**> 1**	**3.5 - 17.5**	**0.5 - 1**	**0.7 - 3.5**	**0.2 - 0.5**	**0.35 - 0.7**	**0.02 - 0.2**	**< 0.35**	**< 0.02**	> 1	1 - 0.2	0.2 - 0.02	2.3	8
2418	Sulphur tetrafluoride	40	20	> **20**	**> 1**	**4 - 20**	**0.5 - 1**	**0.8 - 4**	**0.2 - 0.5**	**0.4 - 0.8**	**0.02 - 0.2**	**< 0.4**	**< 0.02**	> 1	1 - 0.2	0.2 - 0.02	2.3	8
2194	Selenium hexafluoride	50	25	> **25**	**> 1**	**5 - 25**	**0.5 - 1**	**1 - 5**	**0.2 - 0.5**	**0.5 - 1**	**0.02 - 0.2**	**< 0.5**	**< 0.02**	> 1	1 - 0.2	0.2 - 0.02	2.3	8
1589	Cyanogen chloride	80	40	> **40**	**> 1**	**8 - 40**	**0.5 - 1**	**1.6 - 8**	**0.2 - 0.5**	**0.8 - 1.6**	**0.02 - 0.2**	**< 0.8**	**< 0.02**	> 1	1 - 0.2	0.2 - 0.02	2.3	8
1911	Diborane	80	40	> **40**	**> 1**	**8 - 40**	**0.5 - 1**	**1.6 - 8**	**0.2 - 0.5**	**0.8 - 1.6**	**0.02 - 0.2**	**< 0.8**	**< 0.02**	> 1	1 - 0.2	0.2 - 0.02	2.3	2.1
1660	Nitric oxide	115	57.5	> **57.5**	**> 1**	**11.5 - 57.5**	**0.5 - 1**	**2.3 - 11.5**	**0.2 - 0.5**	**1.15 - 2.3**	**0.02 - 0.2**	**< 1.15**	**< 0.02**	> 10	10 - 1	1 - 0.1	2.3	5.1,8
1067	(1)Nitrogedioxide/(2) Dinitrogen tetroxide	115	57.5	> **57.5**	**> 1**	**11.5 - 57.5**	**0.5 - 1**	**2.3 - 11.5**	**0.2 - 0.5**	**1.15 - 2.3**	**0.02 - 0.2**	**< 1.15**	**< 0.02**	> 10	10 - 1	1 - 0.1	2.3	5.1,8
2548	Chlorine pentafluoride	122	61	> **61**	**> 1**	**12.2 - 61**	**0.5 - 1**	**2.44 - 12.2**	**0.2 - 0.5**	**1.22 - 2.44**	**0.02 - 0.2**	**< 1.22**	**< 0.02**	> 1	1 - 0.2	0.2 - 0.02	2.3	5.1,8
2196	Tungsten hexafluoride	160	80	> **80**	**> 1**	**16 - 80**	**0.5 - 1**	**3.2 - 16**	**0.2 - 0.5**	**1.6 - 3.2**	**0.02 - 0.2**	**< 1.6**	**< 0.02**	> 1	1 - 0.2	0.2 - 0.02	2.3	8
1045	Fluorine	185	92.5	> **92.5**	**> 1**	**18.5 - 92.5**	**0.5 - 1**	**3.7 - 18.5**	**0.2 - 0.5**	**1.85 - 3.7**	**0.02 - 0.2**	**< 1.85**	**< 0.02**	> 1	1 - 0.2	0.2 - 0.02	2.3	5.1,8
2198	Phosphorus pentafluoride	190	95	> **95**	**> 1**	**19 - 95**	**0.5 - 1**	**3.8 - 19**	**0.2 - 0.5**	**1.9 - 3.8**	**0.02 - 0.2**	**< 1.9**	**< 0.02**	> 1	1 - 0.2	0.2 - 0.02	2.3	
1017	Chlorine	293	146.5			**29.3 - 100**	**2 - 100**	**5.86 - 29.3**	**1 - 2**	**2.93 - 5.86**	**0.2 - 1**	**< 2.93**	**< 0.2**		> 5	5 - 0.5	2.3	8
1749	Chlorine trifluoride	299	149.5			**29.9 - 100**	**2 - 100**	**5.98 - 29.9**	**1 - 2**	**2.99 - 5.98**	**0.2 - 1**	**< 2.99**	**< 0.2**		> 5	5 - 0.5	2.3	5.1,8
2189	Dichlorosilane	314	157			**31.4 - 100**	**2 - 100**	**6.28 - 31.4**	**1 - 2**	**3.14 - 6.28**	**0.2 - 1**	**< 3.14**	**< 0.2**		> 5	5 - 0.5	2.3	2.1,8
1026	Cyanogen	350	175			**35 - 100**	**2 - 100**	**7 - 35**	**1 - 2**	**3.5 - 7**	**0.2 - 1**	**< 3.5**	**< 0.2**		> 5	5 - 0.5	2.3	2.1
2417	Carbonyl fluoride	360	180			**36 - 100**	**2 - 100**	**7.2 - 36**	**1 - 2**	**3.6 - 7.2**	**0.2 - 1**	**< 3.6**	**< 0.2**		> 5	5 - 0.5	2.3	8
1008	Boron trifluoride	387	193.5			**38.7 - 100**	**2 - 100**	**7.74 - 38.7**	**1 - 2**	**3.87 - 7.74**	**0.2 - 1**	**< 3.87**	**< 0.2**	> 1	1 - 0.2	0.2 - 0.02	2.3	8

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				GHS	EIGA proposal	GHS	EIGA proposal	GHS	EIGA proposal	GHS	EIGA proposal	GHS	EIGA proposal	Very toxic%	Toxic %	Harmful %	Class.	Subs. Risks
3308	Phosphorus trifluoride LC50 FROM ISO 10298	420	210			42 - 100	2 - 100	8.4 - 42	1 - 2	4.2 - 8.4	0.2 - 1	< 4.2	< 0.2		> 5	5 - 0,5	2.3	8
1859	Silicon tetrafluoride	450	225			45 - 100	2 - 100	9 - 45	1 - 2	4.5 - 9	0.2 - 1	< 4.5	< 0.2		> 5	5 - 0,5	2.3	8
2420	Hexafluoroacetone	470	235			47 - 100	2 - 100	9.4 - 47	1 - 2	4.7 - 9.4	0.2 - 1	< 4.7	< 0.2		> 5	5 - 0.5	2.3	8
2192	Germane	620	310			62 - 100	2 - 100	12.4 - 62	1 - 2	6.2 - 12.4	0.2 - 1	< 6.2	< 0.2	> 1	1 - 0.2	0.2 - 0.02	2.3	2.1
1053	Hydrogen sulphide	712	356			71.2 - 100	2 - 100	14.24 - 71.2	1 - 2	7.12 - 14.24	0.2 - 1	< 7.12	< 0.2	> 10	10 - 5	5 - 1	2.3	2.1
1062	Bromomethane	850	425			85 - 100	2 - 100	17 - 85	1 - 2	8.5 - 17	0.2 - 1	< 8.5	< 0.2		> 5	5 - 0.5	2.3	
1052	Hydrogen fluoride	966	483			96.6 - 100	2 - 100	19.32 - 96.6	1 - 2	9.66 - 19.32	0.2 - 1	< 9.66	< 0.2	> 1	1 - 0.2	0.2 - 0.02	8	6.1
3160	Hexafluoro-1,3-Butadiene LC50 UNKNOWN SOURCE	1300	650					26 - 100	5 - 100	13 - 26	0.5 - 5	< 13	< 0.5			> 5	2.3	
1064	Methyl mercaptan	1350	675					27 - 100	5 - 100	13.5 - 27	0.5 - 5	< 13.5	< 0.5			> 5	2.3	2.1
2204	Carbonyl sulphide	1700	850					34 - 100	5 - 100	17 - 34	0.5 - 5	< 17	< 0.5		> 5	5 - 0.5	2.3	2.1
2419	Bromotrifluoroethylene (R113 B1) LC50 UNKNOWN SOURCE	2000	1000					40 - 100	5 - 100	20 - 40	0.5 - 5	< 20	< 0.5			- 5	2.1	
1082	Chlorotrifluoroethylene (R1113)	2000	1000					40 - 100	5 - 100	20 - 40	0.5 - 5	< 20	< 0.5		> 5	5 - 0.5	2.3	2.1
1079	Sulphur dioxide	2520	1260					50.4 - 100	5 - 100	25.2 - 50.4	0.5 - 5	< 25.2	< 0.5		> 20	- 5	2.3	8
1741	Boron trichloride	2541	1270.5					50.82 - 100	5 - 100	25.41 - 50.82	0.5 - 5	< 25.41	< 0.5	> 1	1 - 0.2	0.2 - 0.02	2.3	8
3162	Hexafluoroisobutene LC50 FROM UNKNOWN SOURCE	2650	1325					53 - 100	5 - 100	26.5 - 53	0.5 - 5	< 26.5	< 0.5		> 5	5 - 0.5	2.3	
1050	Hydrogen chloride	2810	1405					56.2 - 100	5 - 100	28.1 - 56.2	0.5 - 5	< 28.1	< 0.5		> 5	5 - 0.5	2.3	8
1048	Hydrogen bromide	2860	1430					57.2 - 100	5 - 100	28.6 - 57.2	0.5 - 5	< 28.6	< 0.5				2.3	8
2197	Hydrogen iodide	2860	1430					57.2 - 100	5 - 100	28.6 - 57.2	0.5 - 5	< 28.6	< 0.5				2.3	8
1040	Ethylene oxide	2900	1450					58 - 100	5 - 100	29 - 58	0.5 - 5	< 29	< 0.5		> 5	5 - 0.5	2.3	2.1
2191	Sulphuryl fluoride	3020	1510					60.4 - 100	5 - 100	30.2 - 60.4	0.5 - 5	< 30.2	< 0.5		> 5	5 - 0.5	2.3	
1016	Carbon monoxide	3760	1880					75.2 - 100	5 - 100	37.6 - 75.2	0.5 - 5	< 37.6	< 0.5		> 5	5 - 0.5	2.3	2.1
1005	Ammonia	4000	2000					80 - 100	5 - 100	40 - 80	0.5 - 5	< 40	< 0.5		> 5	5 - 0.5	2.3	8

UN Nos	Name	LC_{50} 1 h (UN)	LC_{50} 4h (GHS)	CONCENTRATION LIMIT % **category 1**		CONCENTRATION LIMIT % **category 2**		CONCENTRATION LIMIT % **category 3**		CONCENTRATION LIMIT % **category 3**		Non toxic		EU CLASSIFICATION			UN	UN
				GHS	EIGA proposal	GHS	EIGA proposal	GHS	EIGA proposal	GHS	EIGA proposal	GHS	EIGA proposal	Very toxic%	Toxic %	Harmful %	Class.	Subs. Risks
1858	Hexafluoropropene (R1216) LC50 UNKNOWN SOURCE	5600	2800							**56 - 100**	**5 - 100**	**< 56**	**< 5**			5	2.2	
2451	Nitrogen trifluoride LC50 UNKNOWN SOURCE	6700	3350							**67 - 100**	**5 - 100**	**< 67**	**< 5**				2.2	
1061	Methylamine LC50 from ISO10298	7000	3500							**70 - 100**	**5 - 100**	**< 70**	**< 5**			5	2.1	
1083	Trimethylamine LC50 from ISO10298	7000	3500							**70 - 100**	**5 - 100**	**< 70**	**< 5**			5	2.1	
1063	Chloromethane	8300	4150							**83 - 100**	**5 - 100**	**< 83**	**< 5**				2.1	
1032	Dimethylamine LC50 from ISO10298	11000	5500													5	2.1	
2422	Octafluorobutene (R1318) LC50 UNKNOWN SOURCE	12200	6100													5	2.2	
2203	Silane LC50 from ISO10298	19000	9500														2.1	