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
(Seventh session, 14-16 July 2004, agenda item 2)

UPDATING OF THE GLOBALLY HARMONIZED SYSTEM OF CLASSIFICATION AND LABELLING OF CHEMICALS (GHS)

Classification of gas mixtures for toxic effects

Transmitted by the expert from Belgium

1. Introduction

In the GHS, the classification criteria for substances are defined in 3.1.2.1 as:

"3.1.2.1 Chemicals can be allocated to one of five toxicity categories based on acute toxicity by the oral, dermal or inhalation route according to the numeric criteria expressed as (approximate) LD50 (oral, dermal) or LC50 (inhalation) values."

The inhalation toxicity criteria are given in Table 3.1.1 of the GHS;

Table 3.1.1: Acute toxicity hazard categories and (approximate) LC50 values defining the respective categories

Exposure Route		Category 1	Category 2	Category 3	Category 4
Gases (ppmV) *See*	*Note (a)*	100	500	2500	5000
Vapours (mg/l) *See*	*Note (a)* *Note (b)* *Note (c)*	0.5	2.0	10	20
Dusts and Mists (mg/l) *See*	*Note (a)* *Note (d)*	0.05	0.5	1.0	5

The classification criteria for mixtures are defined in 3.1.3.3 as:

"3.1.3.3 In order to make use of all available data for purposes of classifying the hazards of mixtures, certain assumptions have been made and are applied where appropriate in the tiered approach:

(a) The "relevant ingredients" of a mixture are those which are present in concentrations of 1% (w/w for solids, liquids, dusts, mists and vapours and v/v for gases) or greater, unless there is a reason to suspect that an ingredient present at a concentration of less than 1% is still relevant for classifying the mixture for acute toxicity. This point is particularly relevant when classifying untested mixtures which contain ingredients that are classified in Category 1 and Category 2;

(b) The acute toxicity estimate (ATE) for an ingredient in a mixture is derived using:
- The LD50/LC50 where available,
- The appropriate conversion value from Table 3.1.2 that relates to the results of a range test for an ingredient, or
- The appropriate conversion value from Table 3.1.2 that relates to a classification category of the ingredient;

(c) Where a classified mixture is used as an ingredient of another mixture, the actual or derived acute toxicity estimate (ATE) for that mixture may be used when calculating the classification of the new mixture using the formulas in 3.1.3.6.1 and 3.1.3.6.2.3."

NOTE: The concentration value of 1% in 3.1.3.3(a) is inconsistent with the criteria for gases as it is higher than the LC50 concentration value in Table 3.1.1 at which a gaseous substance in air is considered to become non-hazardous (>0.5%).

The ATE of a mixture is determined according to the formula (Dilution Formula) in 3.1.3.6.1:

$$\frac{100}{ATE_{mix}} = \sum_{n} \frac{C_i}{ATE_i}$$

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."

2. ***Inhalation Toxicity and the use of LC50 values***

For inhalation toxicity, exposure is the product of time and concentration of the substance in air. Note (a) to Table 3.1.1 in the GHS, defines the criteria for classification as "Inhalation cut-off values in the table are based on 4 hour testing exposures", therefore the time element in the GHS criteria is fixed. The other element of the GHS classification criteria is the LC50 concentration value referred to in 3.1.2.1. This is the Lethal Concentration of the substance in air at which 50% mortality of the animals in the test occurs. It is important to note that **inhalation toxicity refers to a mixture**.

As the concentration of a mixture of a single substance in air increases above the LC50 (4 hour) value, increased mortality of the animals in the test can be expected to occur to the point where 100% mortality (LC100) will be reached.

As the concentration of the mixture of a single substance in air decreases below the LC50 (4 hour) value, decreased mortality of the animals in the test can be expected to occur to the point where no mortality will occur, and the substance will not be classified as hazardous for inhalation toxicity.

Therefore for a mixture of a single substance in air, there can only be a single (approximate) value at which 50% mortality occurs, and therefore the formula in 3.1.3.6.1 of the GHS can not be applied for inhalation toxicity, as the formula is intended to determine LC50 values at differing concentrations.

As the GHS criteria are based on the (fixed) exposure time of 4 hours and the concentration of the substance in air at which the LC50 value occurs, a single substance will be classified in the GHS hazard category applicable to that LC50 (4 hour) value in the criteria for all concentrations of that single substance above the LC50 concentration value.

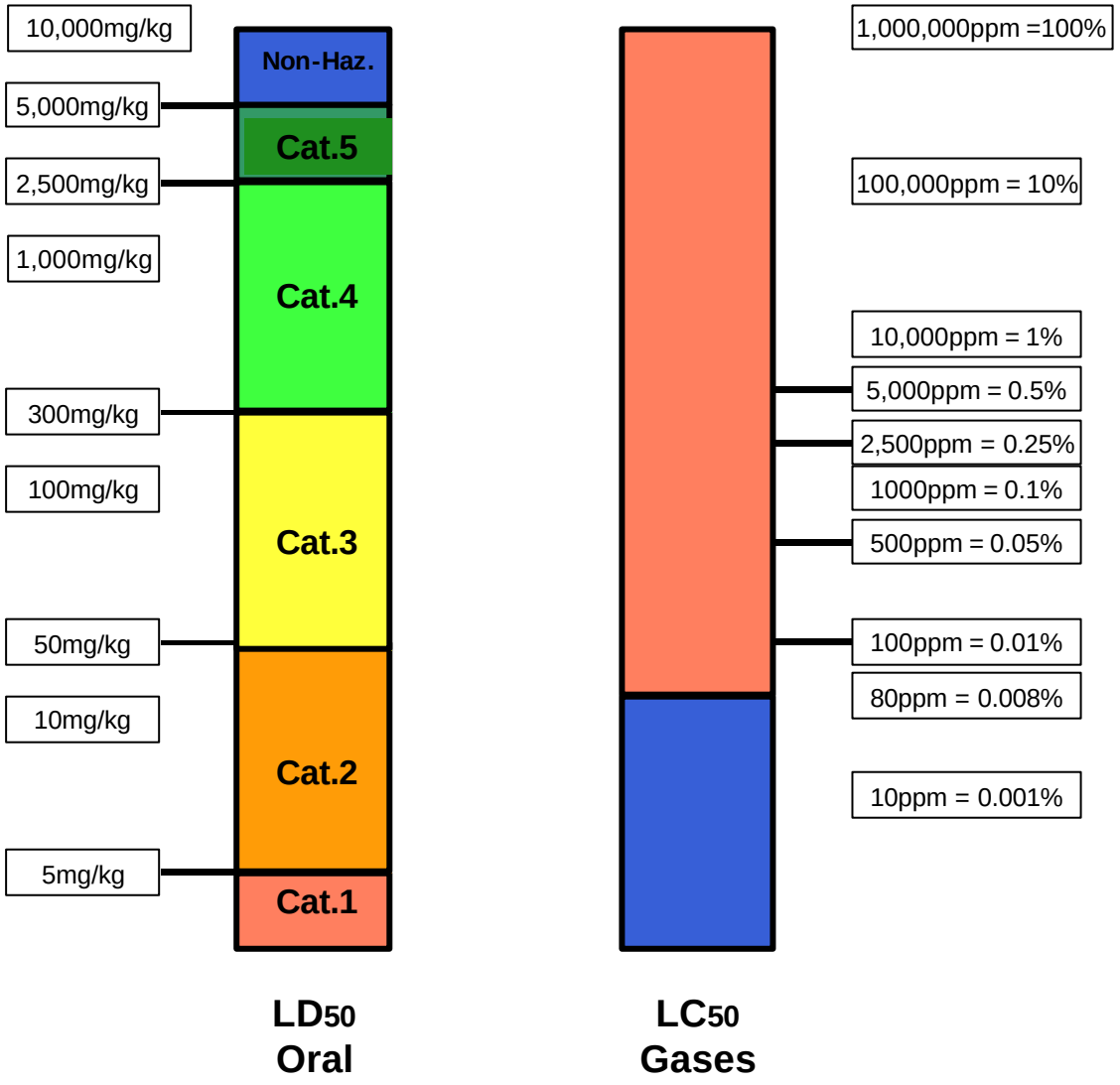
Additionally there is nothing in the GHS criteria which provides a value or measure of equivalence of toxicity of a substance at a higher concentration than the LC50 (4 hour) value, so as to be able to summate toxicities for more than a single substance in a mixture.

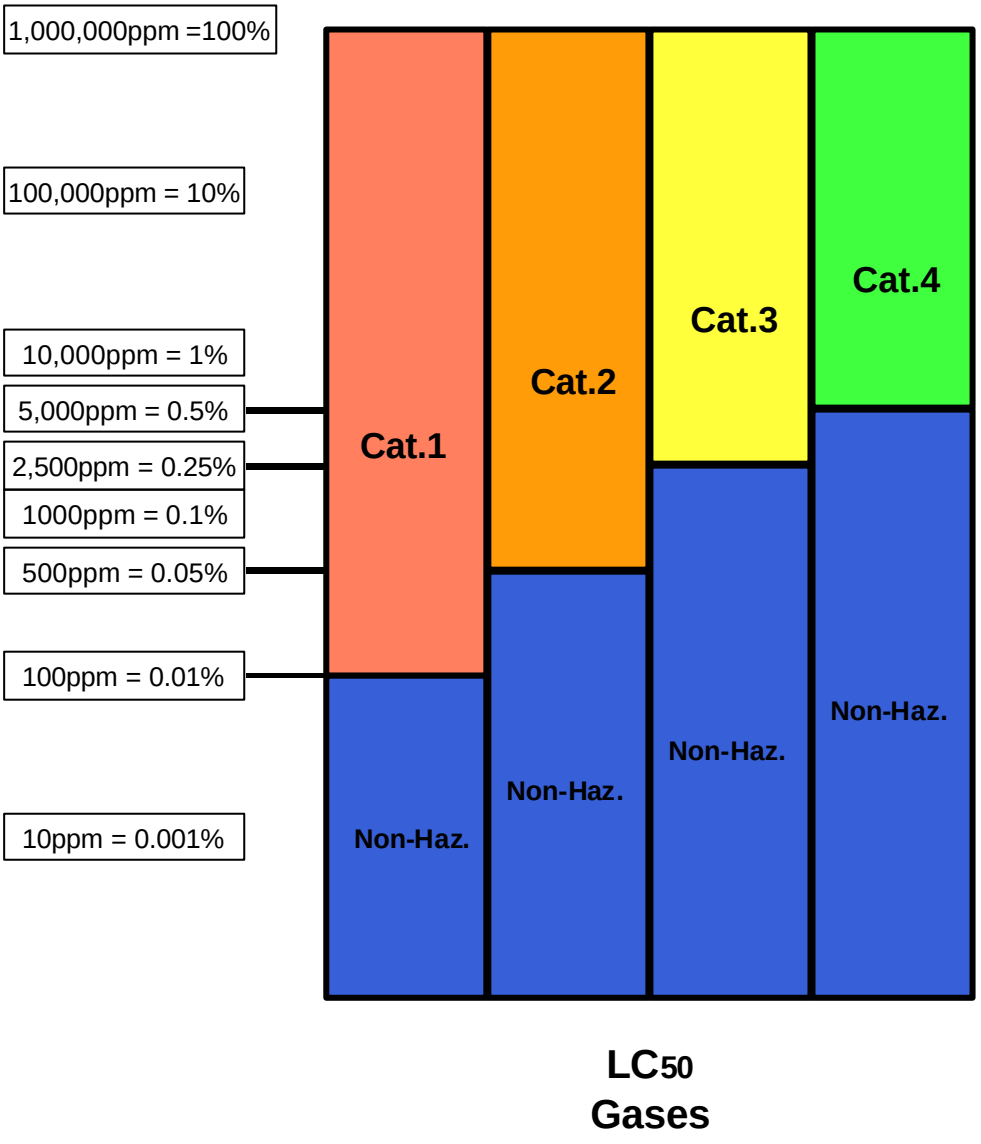
3. Further considerations

In reality there are a number of types of concentrations that need to be taken into account;

(i) experimentally determined concentrations which would theoretically lead to 50% mortality in 4 hours (in a totally enclosed environment)
(ii) concentrations of gas/vapour mixtures in containers in which mixtures are brought to the market
(iii) gas/vapour/dust/mist concentrations to which humans may be exposed in the workplace

CLASSIFICATION OF GAS MIXTURES FOR TOXIC EFFECTS

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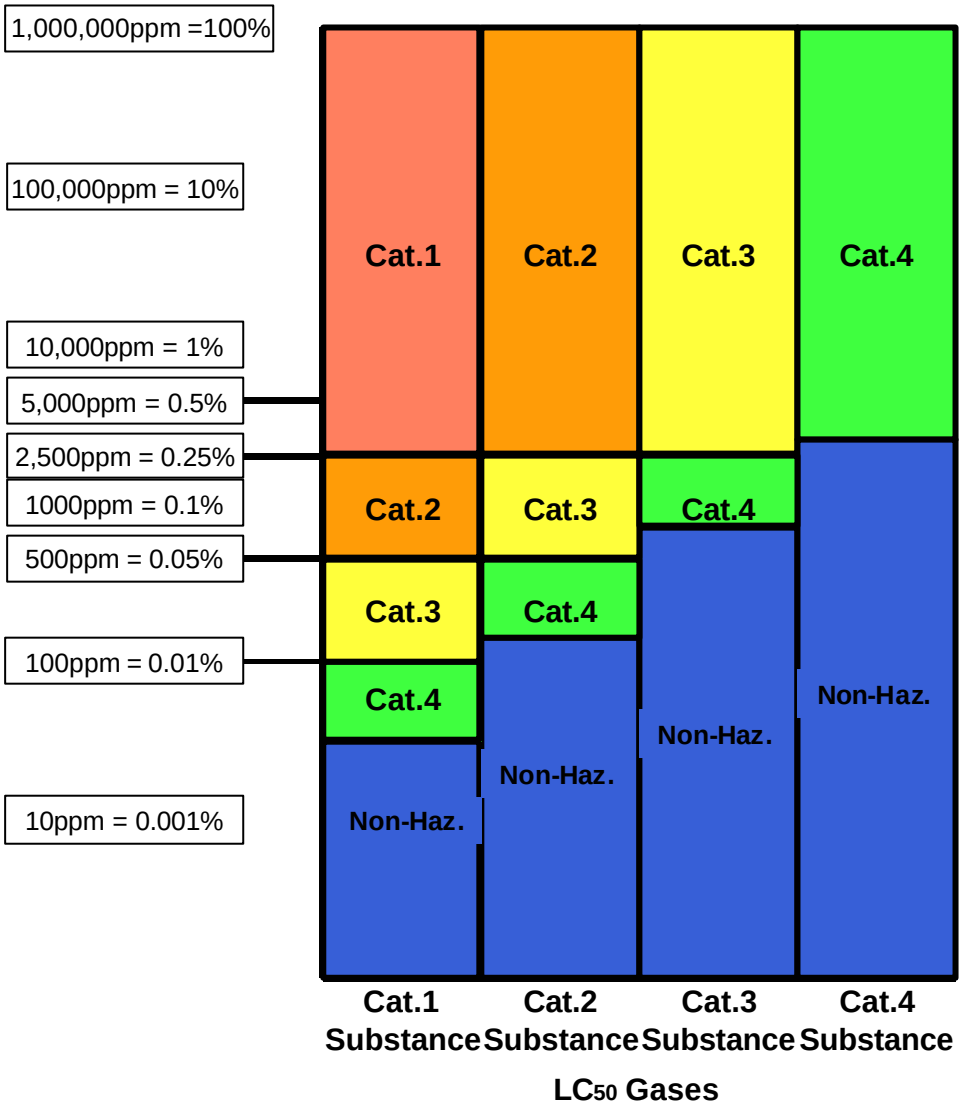
100,000ppm = 10%
10,000ppm = 1%
5,000ppm = 0.5%
2,500ppm = 0.25%
1000ppm = 0.1%
500ppm = 0.05%
100ppm = 0.01%
10ppm = 0.001%
Cat.1
Cat.2
Cat.3
Cat.4
Non-Haz.
Non-Haz.
Non-Haz.
Non-Haz.
LC50
Gases

Table 3.1.1: Acute toxicity hazard categories and (approximate) LD50/LC50 values defining the respective categories

Exposure Route	Category 1	Category 2	Category 3	Category 4
Gases (ppmV) *See: Note (a)*	100	500	2500	5000

Substance in the Mixture	Concentration of the substance in the mixture for classification as				
	sub-category 1	sub-category 2	sub-category 3	sub-category 4	Non-Hazardous
Category 1	C ≥ 2500 C ≥ 0.25%	500<C≤2500 0.05<C≤0.25%	100<C≤ 500 0.01<C≤0.05%	LC_{50}<C≤100 LC_{50}<C≤0.01%	C < LC_{50}
Category 2		C ≥ 2500 C ≥ 0.25%	500<C≤2500 0.05<C≤0.25%	LC_{50}<C≤500 LC_{50}<C≤0.05%	C < LC_{50}
Category 3			C ≥ 2500 C ≥ 0.25%	LC_{50}<C≤2500 LC_{50}<C≤0.25%	C < LC_{50}
Category 4				C ≥ LC_{50}	C < LC_{50}


1,000,000ppm =100%
100,000ppm = 10%
10,000ppm = 1%
5,000ppm = 0.5%
2,500ppm = 0.25%
1000ppm = 0.1%
500ppm = 0.05%
100ppm = 0.01%
10ppm = 0.001%
Cat.1
Cat.2
Cat.3
Cat.4
Cat.2
Cat.3
Cat.4
Cat.3
Cat.4
Cat.4
Non-Haz.
Non-Haz.
Non-Haz.
Non-Haz.
Cat.1 Substance
Cat.2 Substance
Cat.3 Substance
Cat.4 Substance
LC50 Gases