The Globally Harmonized System for Hazard Classification and Communication

Presentation Topic

Classifying Mixtures

in the

Globally Harmonized System

OECD

- Organization for Economic Cooperation and Development

- Technical Focal Point
  - GHS health and environment classification criteria
    - For Substances
    - For Mixtures

The Expert Group for the Classification Criteria for Mixtures

Initial Focus:

Comparison of Existing Systems

The Expert Group Process

- Detailed Review Document
- Approaches Paper
- Proposal for Harmonized Criteria

Agreed Criteria for Mixtures:

» Acute Toxicity

» Sensitization

» Germ Cell Mutagenicity

» Carcinogenicity

» Reproductive Toxicity

» Target Organ Systemic

» Skin and Eye Irritation/Corrosion

» Aquatic Toxicity

Working Definitions

- Mixture:

  Mixtures or solutions composed of two or more substances in which they do not react.

Working Definitions - continued

- Substance:

  Chemical elements and their compounds in the natural state or obtained by any production process.

Working Definitions - continued

- Guidance on the use of hazard classification of a substance:

   Where impurities, additives or individual constituents of a substance have been identified and are themselves classified, they shall be taken into account during classification if they exceed the cut-off value for a given endpoint.

Working Definitions - continued

- Alloy:

An alloy is a metallic material, homogeneous on a macroscopic scale, consisting of two or more elements so combined that they cannot be readily separated by mechanical means.

Alloys are considered to be mixtures for the purpose of classification under the GHS.

The Use of Cut-off Values

Normally,

the harmonized cut-off value is to be applied in all jurisdictions.

However......

The Use of Cut-off Values - Continued

However,

if there is evidence that the hazard of an ingredient is present below the cut-off, then the mixture should be classified accordingly.

Or …..

The Use of Cut-off Values - Continued

...

If there is conclusive data that the hazard of an ingredient will not be present at a level above the harmonized cut-off, then the mixture should be classified accordingly.

Classification Criteria for Mixtures

- Based on the classification criteria for substances

- Allows for the use of available data

The Tier Approach to the Classification of Mixtures

Use test data for the mixture, when available → Use bridging principles, if applicable → Estimate the hazards based on the known information of the ingredient(s)

Acute Toxicity

The "relevant ingredients" in a mixture are present in concentrations of ≥ 1.0%.

Acute Toxicity - continued

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

Where

C_i = concentration of ingredient i

ATE_i = Acute Toxicity Estimate of ingredient i

ATE_{mix} = Acute Toxicity Estimate of the mixture

n ingredients in the mixture and i runs from 1 to n

Acute Toxicity - continued

The Acute Toxicity Estimate (ATE) for an ingredient in a mixture:

– The LD_{50}/LC_{50} where applicable, or

– The appropriate conversion value that relates to:

– the results of a range test for an ingredient, or

– a classification for the ingredient.

Considerations

- Include ingredients with a known acute toxicity which fall into any of the GHS acute toxicity classes.

- Ignore ingredients that are presumed not acutely toxic (e.g.. water, sugar).

Ingredients with Unknown Acute Toxicity

Concentration of unknown ingredients $\leq$ 10%

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

Where

C_i = concentration of ingredient i

ATE_i = Acute Toxicity Estimate of ingredient i

ATE_{mix} = Acute Toxicity Estimate of the mixture

n ingredients in the mixture and i runs from 1 to n

Ingredients with Unknown Acute Toxicity - continued

Concentration of unknown ingredients is > 10%

$$\frac{100 - (\sum C_{i\ unknown} > 10\%)}{ATE_{mix}} = \sum_{n=i} \frac{C_i}{ATE_i}$$

Where

C_i = concentration of ingredient i

ATE_i = Acute Toxicity Estimate of ingredient i

ATE_{mix} = Acute Toxicity Estimate of the mixture

n ingredients in the mixture and i runs from 1 to n

Skin/Eye Corrosion/Irritation

Hazardous to Skin

Sum of ingredients classified as:	Concentration triggering classification of a mixture as:		
	Corrosive	Skin Irritant	
	Class 1	Class 2	Class 3
Skin Class 1	≥ 5 %	≥ 1 % but < 5 %	
Skin Class 2		≥ 10 %	≥ 1 % but < 10 %
Skin Class 3		≥ 10 %	≥ 10 %
(10 x Skin Class 1) + Skin Class 2		≥ 10 %	≥ 1 % but < 10 %
(10 x Skin Class 1) + Skin Class 2 + Skin Class 3			≥ 10 %

Skin/Eye Corrosion/Irritation - continued

Hazardous to the Eye

Sum of Ingredients Classified as:	Concentration triggering classification of a mixture as:	
	Eye	
	Irreversible Class 1	Reversible Class 2
Eye or Skin Class 1	≥3%	≥1% but <3%
Eye Class 2/2A		≥10%
(10 x Eye Class 1) + Eye Class 2/2A		≥10%
Skin Class 1 + Eye Class 1	≥3%	≥1% but <3%
10 x (Skin Class 1 + Eye Class 1) + Eye Class 2/2A		≥10%

Skin/Eye Corrosion/Irritation - continued

If the additivity approach does not apply...

Ingredient:	Conc	Mixture classified as:	
		Skin	Eye
Acid with pH ≤ 2	≥ 1%	Class 1	Class 1
Base with pH ≥11.5	≥ 1%	Class 1	Class 1
Other corrosive (Class 1) ingredients for which additivity does not apply	≥ 1%	Class 1	Class 1
Other irritant (Class 2) ingredients for which additivity does not apply, including acids and bases	≥ 3%	Class 2	Class 2

Respiratory and Skin Sensitization

Ingredient Classified as	Cut-off value triggering classification of a mixture as a	
	Skin Sensitizer	Respiratory Sensitizer
Skin Sensitizer	$\geq 1.0\%$ (Solid/Liquid) $\geq 1.0\%$ (Gas)	-
Respiratory Sensitizer	-	$\geq 1.0\%$ (Solid/Liquid) $\geq 0.2\%$ (Gas)

Mutagenicity

Ingredient Classified as	Cut-off value triggering classification of a mixture as a	
	Class 1 Mutagen	Class 2 Mutagen
Class 1 Mutagen	≥0.1%	-
Class 2 Mutagen	-	≥1.0%

Carcinogenicity

Ingredient Classified as	Cut-off Value triggering Classification of a mixture as a	
	Class 1 Carcinogen	Class 2 Carcinogen
Class 1 Carcinogen	≥0.1 %	-
Class 2 Carcinogen	-	≥0.1% (note 1) --------- ≥1.0% (note 2)

Note 1 and 2:
Refer to the Step 2 Proposal for Harmonized Classification Criteria for Mixtures

Carcinogenicity – Hazard Communication

Hazard Communication	Mixture Classified as a	
	Class 1 Carcinogen	Class 2 Carcinogen
MSDS	≥0.1 %	≥0.1 %
Label	≥0.1 %	≥0.1% (note) ----- ≥1.0% (note)

Note:

Some authorities will choose to label Class 2 carcinogens at ≥0.1 % while others will choose to label Class 2 carcinogens at ≥1.0%

Reproductive Toxicity

Ingredient Classified as	Cut-off value triggering classification of a mixture as a	
	Class 1 Reproductive Toxicant	Class 2 Reproductive Toxicant
Class 1 Reproductive Toxicant	$\leq$0.1 % (note 1) -------- $\leq$0.3 % (note 2)	$\leq$0.1 % (note 3) -------- $\leq$3.0 % (note 4)
Class 2 Reproductive Toxicant	-	

Notes 1-4: Refer to the Step 2 Proposal for Harmonized Classification Criteria for Mixtures

Reproductive Toxicity - Hazard Communication

Hazard Communication	Mixture Classified as:	
	Class 1 Reproductive Toxicant	Class 2 Reproductive Toxicant
MSDS	≥ 0.1 %	≥ 0.1 %
Label	$\geq 0.1\%$ (note) ------ $\geq 0.3\%$ (note)	$\geq 0.1\%$ (note) ------ $\geq 3.0\%$ (note)

Note: Some authorities will choose to label Class 1 reproductive toxicants at ≥ 0.1 % while others will label this class at $\geq 0.3\%$.

Similarly, some authorities will choose to label Class 2 reproductive toxicants at ≥ 0.1 % while others will label this class at $\geq 3.0\%$

Target Organ Systemic Toxicity (TOST)

Ingredient Classified as	Cut-off value triggering classification of a mixture as a	
	Class 1 TOST	Class 2 TOST
Class 1 TOST	⩾1.0 % (note 1)	-
	⩾10 % (note 2)	⩾1.0 % (note 3)
Class 2 TOST	-	⩾1.0 % (note 4)
		⩾10.0 % (note 5)

Notes 1-5: Refer to the Step 2 Proposal for Harmonized Classification Criteria for Mixtures

TOST - Hazard Communication

Hazard Communication	Mixture Classified as:	
	Class 1 TOST	Class 2 TOST
MSDS	≤1.0 %	≤1.0 %

TOST - Hazard Communication

Hazard Communication	Mixture Classified as:	
	Class 1 TOST	**Class 2 TOST**
	≥1.0%	≥1.0 %
Label	≥10.0 %	1.0% ≤ Class 1 TOST Mixture <10.0% ≥10.0 %

TOST - Hazard Communication

Note: Class 1 –

Some authorities will label mixtures with Class 1 ingredients $\leq$1.0 %. Others will label mixtures with Class 1 TOST ingredients at $\leq$1.0 %.

Class 2 –

Some authorities will label mixtures with Class 2 ingredients $\leq$1.0 % while others will label mixtures with Class 2 TOST ingredients at $\leq$10.0%.

Further, if an authority uses the 10% cut-off for Class 1 but the ingredient is present in the mixture between 1.0% and 10.0%, these authorities will label this mixture as a Class 2 TOST.

Aquatic Toxicity

Data available for the mixture as a whole:

- Classify based on the cut-offs established for:

  - LC_{50}
  - EC_{50}
  - NOEC
  - Water solubility

Aquatic Toxicity - continued

Sufficient data on similar mixtures:

Apply Bridging Principles

Aquatic Toxicity - continued

Aquatic Toxicity or Classification Data available for all relevant components?

Consider:

- % components classified as chronic
- % components classified as acute % components with acute toxicity data, and
- % component with acute toxicity data, and ...

Aquatic Toxicity - continued

Aquatic toxicity or classification data available for all relevant components?

... Add the concentrations of the classified components and apply threshold values to classify the mixture.

Hazard Data available on known components?

Depending on the what is known about

the components either:

Add the concentrations of classified

components and apply threshold value

to classify,

or …

Aquatic Toxicity - continued

Hazard Data available on known components?

$$\frac{\sum c_i}{L(E)C_{50m}} = \sum_{\eta} \frac{c_i}{L(E)C_{50i}}$$

where:

C_I = concentration of component i (weight percentage)

$L(E)C_{50i}$ = (mg/L) LC_{50} or EC_{50} for component I

η = number of components

$L(E)C_m$ = $L(E)$ C_{50} of the part of the mixture with test data

Physical Hazards

It is assumed that mixtures will be tested for physical hazards.

The Globally Harmonized System for Hazard Classification and Communication