Image: Gemini

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Classifying mixtures in the GHS

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Agenda

- Kick off questions
- Defining which elements to include in a label
- Classification of a mixture
- Classification of Physical Hazards (need to test)
- Classification of Health and Environmental Hazards (tiered approach)
- Summing up

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KICK OFF QUESTIONS

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Defining which elements to include in a label

LABELS IN MIXTURES:

The GHS uses labels to communicate chemical hazards.

The labelling elements for mixtures are the same as those used for substances

Isobiocide C10

Contains:
reaction mass of 5-chloro-2-methyl-2*H*-isothiazol-3-one and 2-methyl-2*H*-isothiazol-3-one (3:1)

BATCH Nº 035/2025

1 Liter

PICTOGRAMS

DANGER

SIGNAL WORD

HAZARD STATEMENTS

Toxic if swallowed
Fatal in contact with skin
Fatal if inhaled
Causes severe skin burns and eye damage
May cause an allergic skin reaction
Very toxic to aquatic life with long lasting effects

Do not get in eyes, on skin, or on clothing.
Wash hands thoroughly after handling. Do not touch eyes.
Wear protective gloves/protective clothing/eye protection/face protection.
In case of inadequate ventilation wear respiratory protection.
IF SWALLOWED: rinse mouth. Do not induce vomiting.
IF ON SKIN (or hair): take off immediately all contaminated clothing. Immediately rinse with water for several minutes.
IF INHALED: remove person to fresh air and keep comfortable for breathing.
IF IN EYES: immediately rinse with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
Get emergency medical help immediately.
If skin irritation or rush occurs: get medical help.
Avoid release to the environment. Collect spillage.
Store locked up.
Dispose of contents/container in accordance with local regulation.

PRECAUTIONARY STATEMENTS

Manufactured by CHEMCOM DAC
Abcde 1111, Córdoba,
ARGENTINA
Phone Nº +54 351 1111-1111
www.chemcomdac.com.ar

Elaborated by J. Bensignor

DEFINITION OF LABELLING ELEMENTS

unitar course on Classification and labelling available

The labelling elements to include for a mixture (or a substance) are determined **based on its hazard classification.**

For each hazard class, the **Purple Book** indicates which elements must appear on a label according to the classification results.

Definition of labelling elements

Isobiocide C10 example

Isobiocide C10

Contains:
reaction mass of 5-chloro-2-methyl-2*H*-isothiazol-3-one and 2-methyl-2*H*-isothiazol-3-one (3:1)

BATCH Nº 035/2025

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PICTOGRAM

DANGER ← SIGNAL WORD

HAZARD STATEMENT →

Toxic if swallowed
Fatal in contact with skin
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Causes severe skin burns and eye damage
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Do not get in eyes, on skin, or on clothing.
Wash hands thoroughly after handling. Do not touch eyes.
Wear protective gloves/protective clothing/eye protection/face protection.
In case of inadequate ventilation wear respiratory protection.
IF SWALLOWED: rinse mouth. Do not induce vomiting.
IF ON SKIN (or hair): take off immediately all contaminated clothing. Immediately rinse with water for several minutes.
IF INHALED: remove person to fresh air and keep comfortable for breathing.
IF IN EYES: immediately rinse with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
Get emergency medical help immediately.
If skin irritation or rush occurs: get medical help.
Avoid release to the environment. Collect spillage.
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Definition of labelling elements

Isobiocide C10 example

Table 3.2.5: Label elements for skin corrosion/irritation

	Category 1			Category 2	Category 3
	1 A	1 B	1 C		
Symbol	Corrosion	Corrosion	Corrosion	Exclamation mark	*No symbol*
Signal word	Danger	Danger	Danger	Warning	Warning
Hazard statement	Causes severe skin burns and eye damage	Causes severe skin burns and eye damage	Causes severe skin burns and eye damage	Causes skin irritation	Causes mild skin irritation

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Classifying a mixture

What hazard information for the mixture is available?

EXPERIMENTAL DATA FOR THE COMPLETE MIXTURE IS AVAILABLE

Classification must be based on the **experimental data**

unitar course on Classification and labelling available

EXPERIMENTAL DATA FOR THE COMPLETE MIXTURE IS NOT AVAILABLE

Classification must follow the **criteria outlined** in the Purple Book **for each hazard group**

HEALTH AND ENVIRONMENTAL HAZARDS

TIERED APPROACH

1. Use data on the complete mixture
2. Use data on similar mixtures → **BRIDGING PRINCIPLES**
3. Use data on ingredients → **ADDITIVE AND NON ADDITIVE CONTRIBUTIONS**

PHYSICAL HAZARDS

NEED TO TEST

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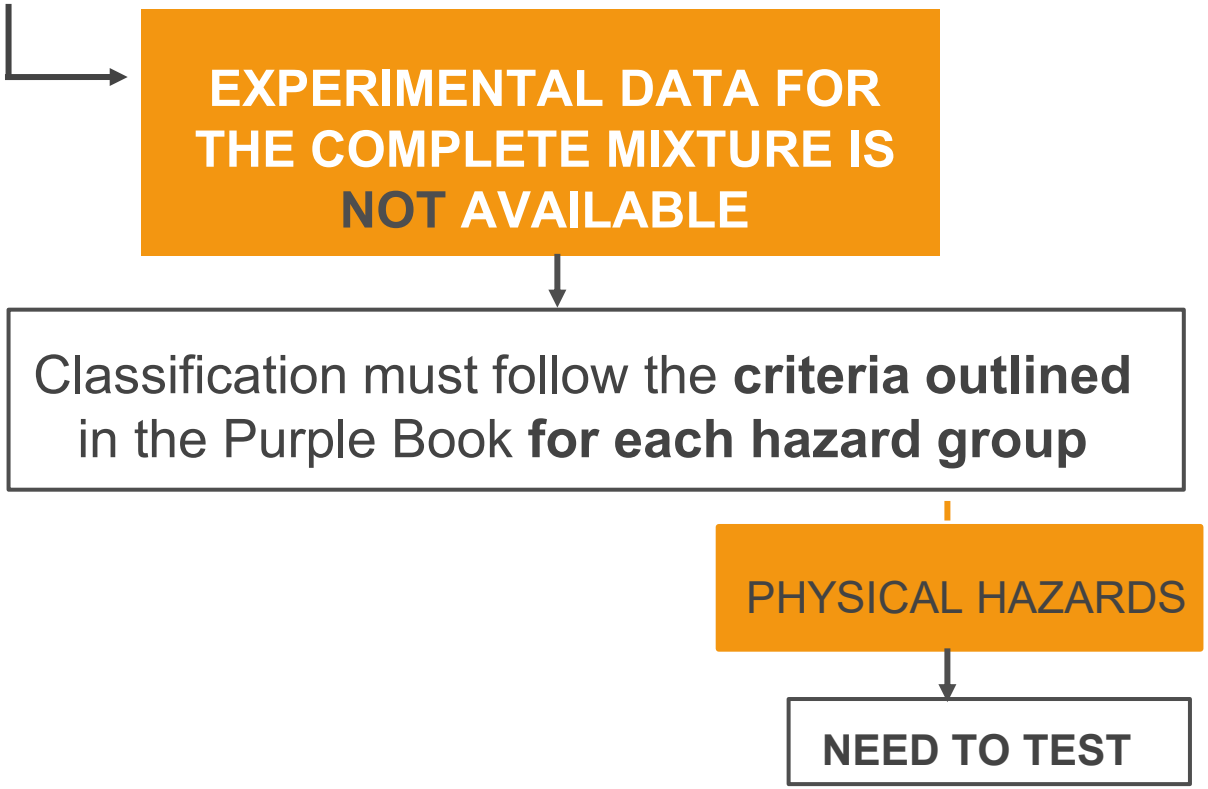
Classification of Physical Hazards
(need to test)

What hazard information for the mixture is available?



Classification of mixtures: Physical Hazards

Need to test the complete mixture

PHYSICAL HAZARDS IN MIXTURES

- For physical hazards, classification always requires data for the complete mixture
- If no data are available for the mixture, it must be tested for each hazard class.
- The classification procedures are the same as those used for substances.

Classification of mixtures: Physical Hazards

Need to test the complete mixture

PHYSICAL HAZARDS IN MIXTURES
EXAMPLE

Flash point: 18ºC
Initial boiling point: 52ºC

Table 2.6.1: Criteria for flammable liquids

Category	Criteria
1	Flash point < 23 °C and initial boiling point ≤ 35 °C
2	Flash point < 23 °C and initial boiling point > 35 °C
3	Flash point ≥ 23 °C and ≤ 60 °C
4	Flash point > 60 °C and ≤ 93 °C

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Classification of Health and Environmental Hazards
(tiered approach)

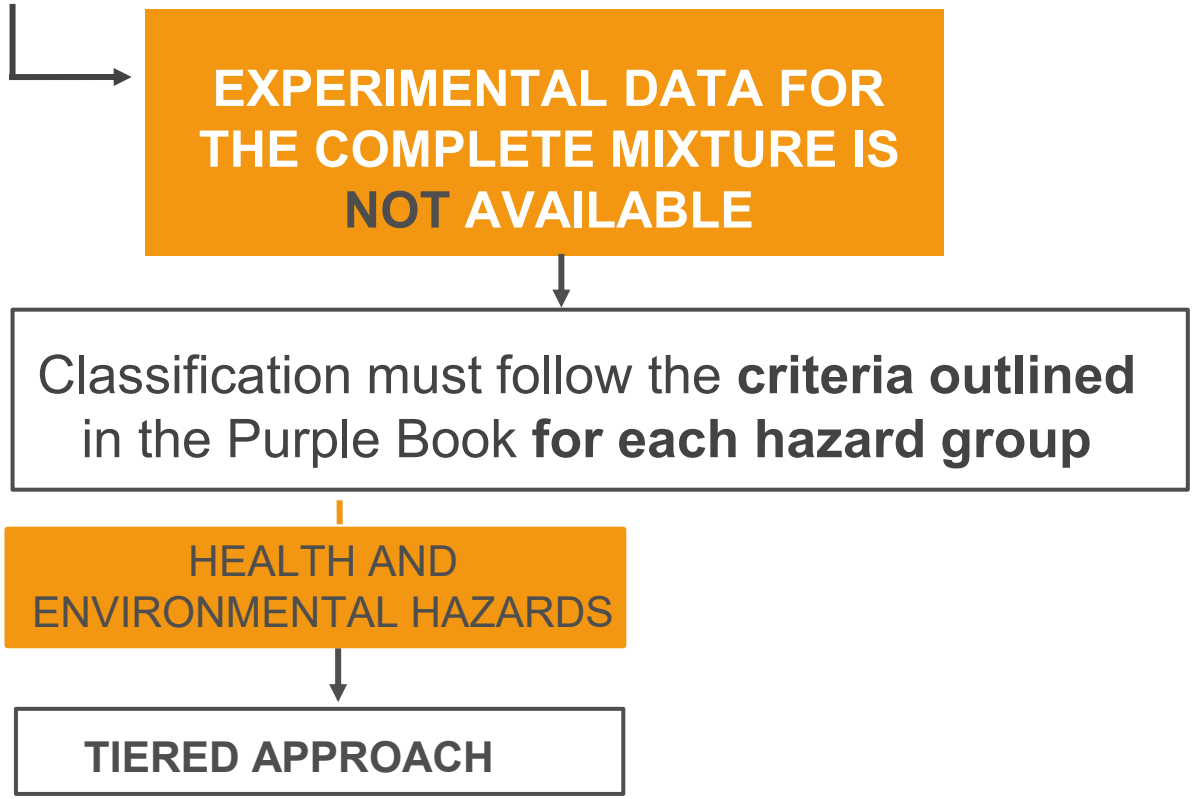
What hazard information for the mixture is available?

EXPERIMENTAL DATA FOR THE COMPLETE MIXTURE IS NOT AVAILABLE

Classification must follow the **criteria outlined** in the Purple Book **for each hazard group**

HEALTH AND ENVIRONMENTAL HAZARDS

What hazard information for the mixture is available?



TIERED APPROACH
(for health and environmental hazards)

1. Use available test data for the complete mixture

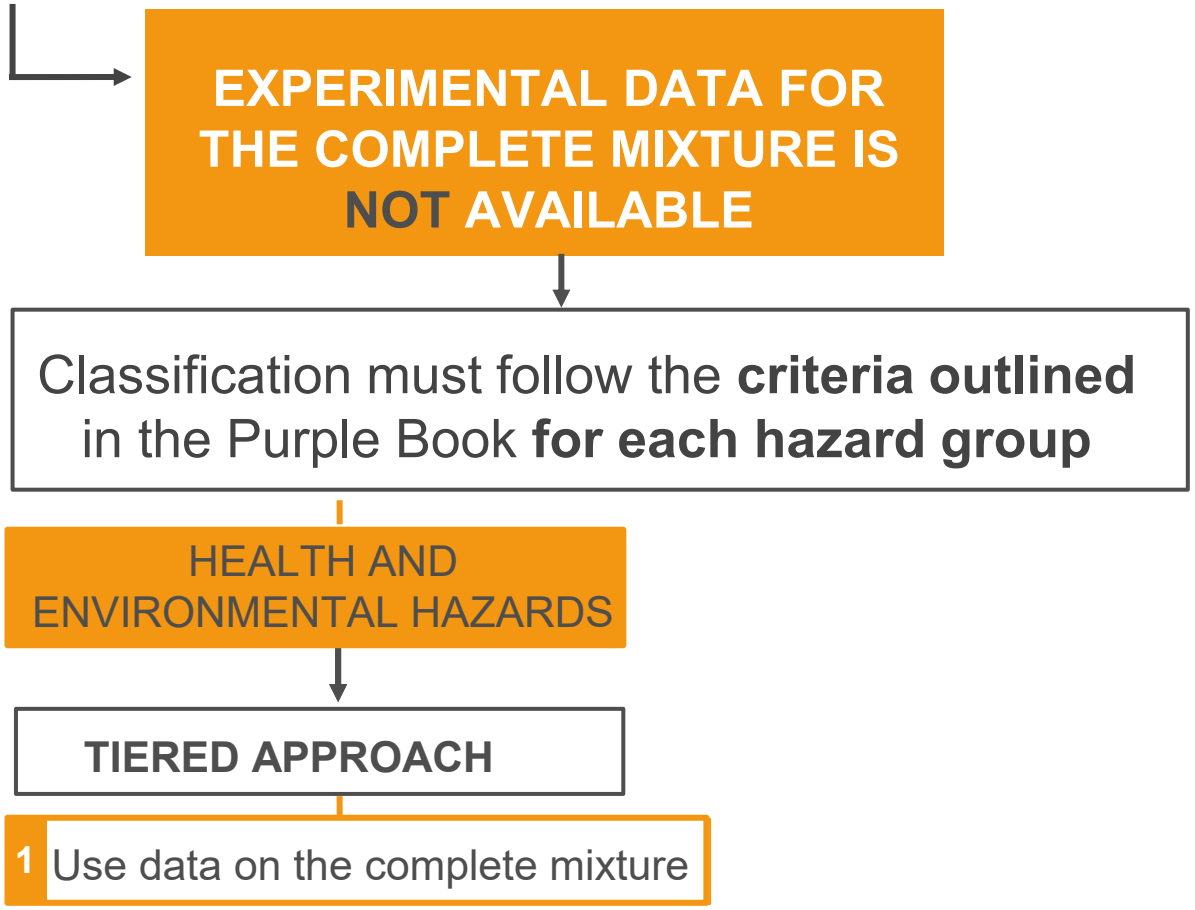
(if not available)

2. Use available test data for similar mixtures

(if not available)

3. Use available data on ingredients

What hazard information for the mixture is available?



Classification of mixtures: Health and Environmental hazards

EXAMPLE

1 Use available test data for the complete mixture

Table 4.1.1: Categories for substances hazardous to the aquatic environment *(Note 1)*

(a) Short-term (acute) aquatic hazard

Category Acute 1: *(Note 2)*	
96 hr LC_{50} (for fish)	≤ 1 mg/l and/or
48 hr EC_{50} (for crustacea)	≤ 1 mg/l and/or
72 or 96hr ErC_{50} (for algae or other aquatic plants)	≤ 1 mg/l *(Note 3)*
Category Acute 1 may be subdivided for some regulatory systems to include a lower band at $L(E)C_{50}$ ≤ 0.1 mg/l	
Category Acute 2:	
96 hr LC_{50} (for fish)	> 1 but ≤ 10 mg/l and/or
48 hr EC_{50} (for crustacea)	> 1 but ≤ 10 mg/l and/or
72 or 96hr ErC_{50} (for algae or other aquatic plants)	> 1 but ≤ 10 mg/l *(Note 3)*
Category Acute 3:	
96 hr LC_{50} (for fish)	> 10 but ≤ 100 mg/l and/or
48 hr EC_{50} (for crustacea)	> 10 but ≤ 100 mg/l and/or
72 or 96hr ErC_{50} (for algae or other aquatic plants)	> 10 but ≤ 100 mg/l *(Note 3)*
Some regulatory systems may extend this range beyond an $L(E)C_{50}$ of 100 mg/l through the introduction of another category.	

LC50 (96 hr) fish: 7.5 mg/L
EC50 (72 hr) crustacea: 2.5 mg/L
ErC50 (72 hr) algae: 12.4 mg/L

ACTIVITY

Source: Gemini

ACTIVITY

Classify MIXTURE Z for **Acute toxicity** using the following data and GHS criteria

LD50 oral 6500 mg/kg
LD50 dermal 150 mg/kg
LC50 inhalation 3500 ppmV

Table 3.1.1: Acute toxicity estimate (ATE) values and criteria for acute toxicity hazard categories

Exposure route	Category 1	Category 2	Category 3	Category 4	Category 5
Oral (mg/kg bodyweight) *See notes (a) and (b)*	ATE ≤ 5	5 < ATE ≤ 50	50 < ATE ≤ 300	300 < ATE ≤ 2000	2000< ATE≤ 5000 *See detailed criteria in note (g)*
Dermal (mg/kg bodyweight) *See notes (a) and (b)*	ATE ≤ 50	50 < ATE ≤ 200	200 < ATE ≤ 1000	1000 < ATE ≤ 2000	
Gases (ppmV) *See notes (a), (b) and (c)*	ATE ≤ 100	100 < ATE ≤ 500	500 < ATE ≤ 2500	2500 < ATE ≤ 20000	*See detailed criteria in note (g)*
Vapours (mg/l) *See notes (a), (b), (c), (d) and (e)*	ATE ≤ 0.5	0.5 < ATE ≤ 2.0	2.0 < ATE ≤ 10.0	10.0 < ATE ≤ 20.0	
Dusts and Mists (mg/l) *See notes (a), (b), (c) and (f)*	ATE ≤ 0.05	0.05 < ATE ≤ 0.5	0.5 < ATE ≤ 1.0	1.0 < ATE ≤ 5.0	

ACTIVITY

Classify MIXTURE Z for **Acute toxicity** using the following data and GHS criteria

LD50 oral 6500 mg/kg
LD50 dermal 150 mg/kg
LC50 inhalation 3500 ppmV

Table 3.1.1: Acute toxicity estimate (ATE) values and criteria for acute toxicity hazard categories

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Dermal (mg/kg bodyweight) *See notes (a) and (b)*	ATE ≤ 50	50 < ATE ≤ 200	200 < ATE ≤ 1000	1000 < ATE ≤ 2000	
Gases (ppmV) *See notes (a), (b) and (c)*	ATE ≤ 100	100 < ATE ≤ 500	500 < ATE ≤ 2500	2500 < ATE ≤ 20000	*See detailed criteria in note (g)*
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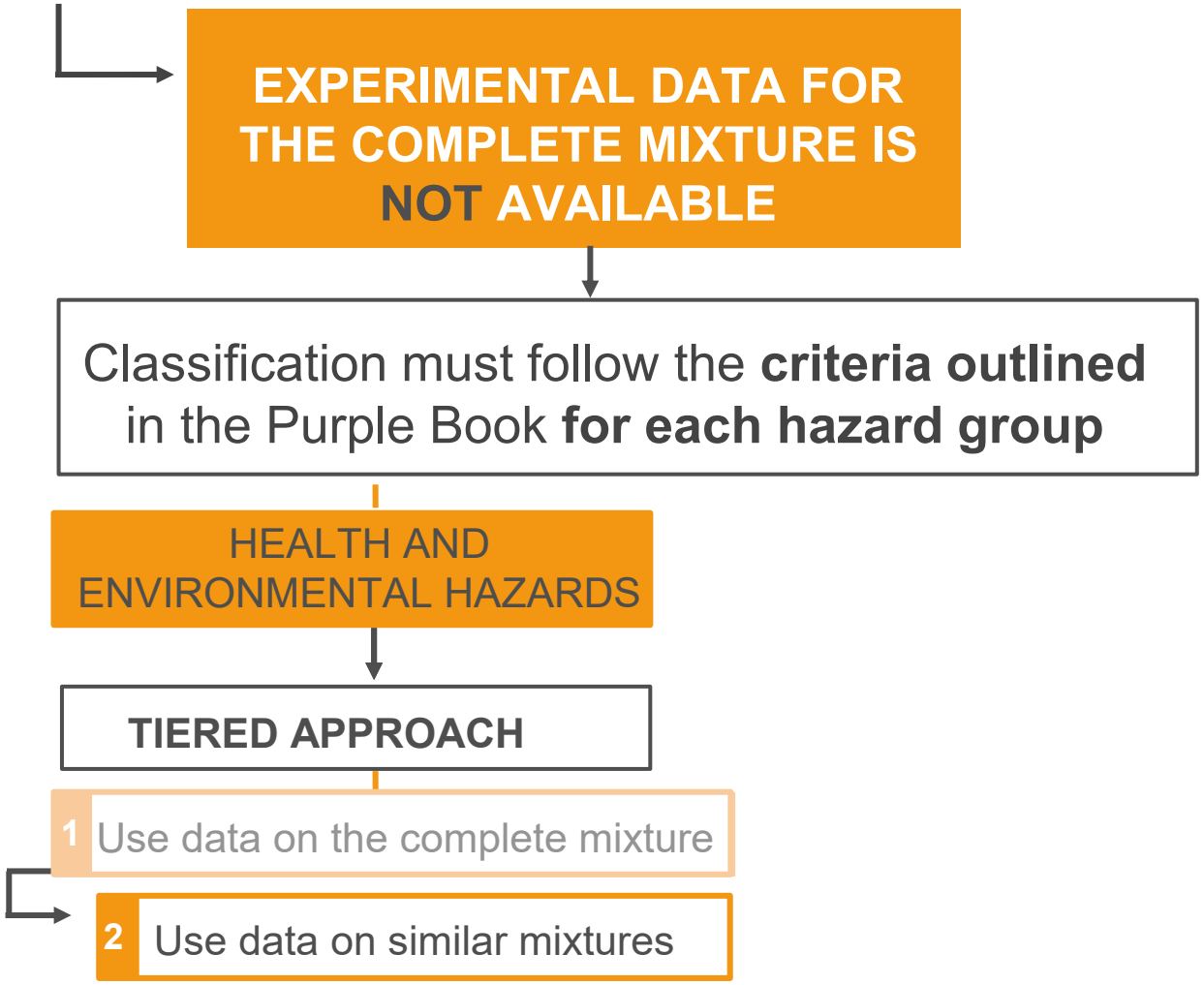
Dusts and Mists (mg/l) *See notes (a), (b), (c) and (f)*	ATE ≤ 0.05	0.05 < ATE ≤ 0.5	0.5 < ATE ≤ 1.0	1.0 < ATE ≤ 5.0	

ORAL: not classified

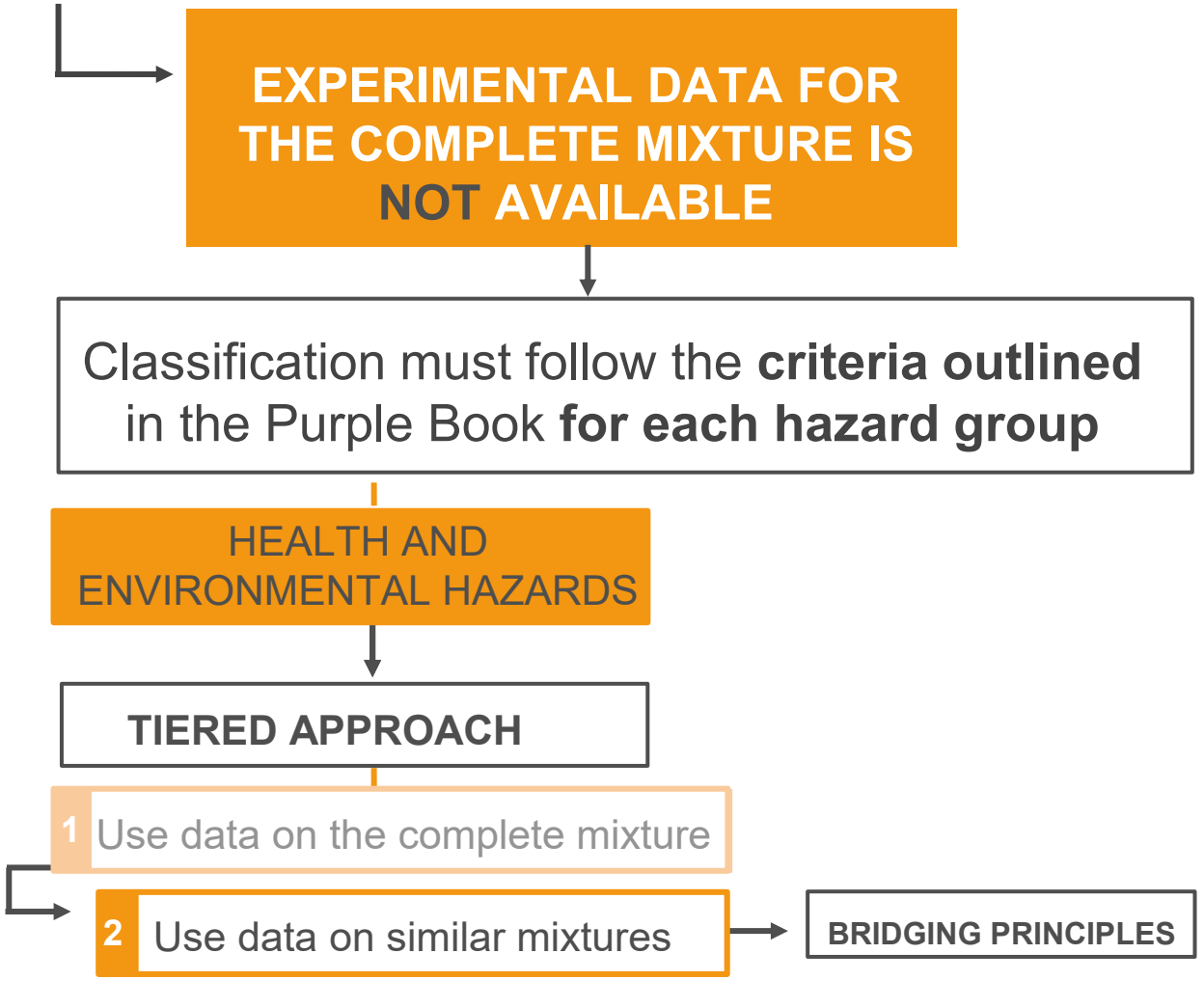
DERMAL: CAT. 2

INHALATION (GASES): CAT. 4

What hazard information for the mixture is available?



What hazard information for the mixture is available?



BRIDGING PRINCIPLES

in the absence of data on the complete mixture, the GHS proposes the use of data on similar mixtures

(containing the same or similar hazardous ingredients as the mixture being classified).

the Purple Book establishes bridging principles for each hazard class.

Classification of mixtures: Health and Environmental hazards

Tiered approach

2 Use available test data for similar mixtures
BRIDGING PRINCIPLES

- **DILUTION**
- **BATCHING**
- **CONCENTRATION of highly hazardous mixtures**
- **INTERPOLATION within one hazard category**
- **SUBSTANTIALLY SIMILAR MIXTURES**
- **AEROSOLS**

Classification of mixtures: Health and Environmental hazards

Bridging principles

2 Use available test data for similar mixtures **DILUTION**

If a tested mixture is diluted with a diluent that has the same or lower toxicity than its own least toxic original ingredient

(and that is not expected to affect the toxicity of its other ingredients)

the new diluted mixture can be classified the same as the original mixture

Classification of mixtures: Health and Environmental hazards

Bridging principles

Use available test data for similar mixtures
DILUTION

Example: If *Mixture 1* is classified as Skin Irritant Category 2, and is diluted with water

(which is not a skin irritant and doesn't chemically react),

the new mixture (*Mixture 2*) should also be classified as Skin Irritant Category 2 (based on Mixture 1), unless further analysis shows it no longer meets the criteria.

Classification of mixtures: Health and Environmental hazards

Bridging principles

2 Use available test data for similar mixtures **BATCHING**

The hazard classification of a tested batch can be applied to untested batches of the same mixture when:

- the batches are produced under controlled conditions, and
- the production is performed under the same manufacturer control, and
- there is no reason to believe that the toxicity of the untested mixture has changed.

Classification of mixtures: Health and Environmental hazards

Bridging principles

2 Use available test data for similar mixtures **BATCHING**

Example: Two batches of a paint (Batch X and Batch Y) are produced using:

- the same process,
- the same raw materials,
- with only slight variations in ingredient concentrations within a defined tolerance

If Batch X is tested and classified, Batch Y can assume the same classification.

Classification of mixtures: Health and Environmental hazards

Bridging principles

2 Use available test data for similar mixtures
CONCENTRATION OF HIGHLY HAZARDOUS MIXTURES

- If a mixture is classified in the highest hazard category for a particular hazard class, and
- the concentration of the hazardous ingredient(s) is increased,

the new, more concentrated mixture must also be classified in the same highest hazard category.

Classification of mixtures: Health and Environmental hazards

Bridging principles

2 Use available test data for similar mixtures
CONCENTRATION OF HIGHLY HAZARDOUS MIXTURES

Example: If *Mixture 1*, containing Substance X (a Category 1 skin sensitizer), is

- classified as Skin Sensitization Category 1 due to the presence of Substance X, and
- a new *Mixture 2* is created with a higher concentration of Substance X,

***Mixture 2* would also be classified as Skin Sensitization Category 1.**

Classification of mixtures: Health and Environmental hazards

Bridging principles

2 Use available test data for similar mixtures **INTERPOLATION (within one hazard category)**

- If two tested mixtures (*Mixtures 1* and *2)* with the same hazardous ingredient(s), are classified in the same category for a specific hazard, and

- an untested *Mixture 3* contains the same hazardous ingredient(s)
- at concentrations sitting between those of *Mixtures 1 and 2*

then *Mixture 3* is assumed to be in that same hazard category.

Classification of mixtures: Health and Environmental hazards

Bridging principles

2 Use available test data for similar mixtures **INTERPOLATION (within one hazard category)**

Example: If *Mixture 1* (5% of Ingredient X) and *Mixture 2* (15% of Ingredient X) are

- both classified as Acute Toxicity (oral) Category 3, and
- *Mixture 3* has 10% of Ingredient X

then *Mixture 3* would also be classified as Acute Toxicity (oral) Category 3, (assuming Ingredient X is the sole or dominant contributor to that hazard.)

Classification of mixtures: Health and Environmental hazards

Bridging principles

2 Use available test data for similar mixtures
SUBSTANTIALLY SIMILAR MIXTURES

For two Mixtures *(A + B)* and *(A + C)* where:

- 'A' is present in both mixtures at the same concentrations, and
- data on toxicity is available for 'B' and for 'C', being substantially equivalent in their hazard characteristics, and
- *Mixture (A + B)* is classified based on test data,

then *Mixture (A + C)* can be assumed to have the same classification.

Classification of mixtures: Health and Environmental hazards

Bridging principles

2 Use available test data for similar mixtures
SUBSTANTIALLY SIMILAR MIXTURES

The product Super Bleach is sold in two versions, one with strawberry fragrance and another with lemon fragrance, both using the same base formulation. If:

- Super Bleach strawberry version is classified as a Skin Irritant Category 2 based on test data, and
- both fragrances (both ingredients) have the same skin irritation classification and are present at the same concentration,

then the Super Bleach lemon version can also be classified equally as a Skin Irritant Category 2

Classification of mixtures: Health and Environmental hazards

Bridging principles

2 Use available test data for similar mixtures
AEROSOLS

An aerosol mixture is considered to have the same classification as its non-aerosolized form, provided that:

- the propellant was classified and does not affect the hazards of the mixture for the oral and dermal exposition route.
- If the propellant contributes to a hazard, that hazard must also be considered.

For the inhalation route toxicity must be evaluated separately)

Classification of mixtures: Health and Environmental hazards

Bridging principles

2 Use available test data for similar mixtures
AEROSOLS

Example:

A liquid disinfectant classified as a Skin Corrosive will retain that classification if packaged as an aerosol, **unless the propellant changes its corrosive properties.**

ACTIVITY

Source: Gemini

ACTIVITY

Classify a mixture using bridging principles

- Classify MIXTURE 2 for Skin Corrosion/Irritation using bridging principles based on information for MIXTURE 1 and indicate on which of the bridging principles the classification is based.

MIXTURE 1

MIXTURE 1 Classification for Skin Corrosion/Irritation: Category 1 (based on conclusive data for the whole mixture)

Substance B: Skin Corrosion/Irritation classification: Category 1

MIXTURE 2

MIXTURE 2 Classification for Skin

Corrosion/Irritation: **?**

Substance C: Skin Corrosion/Irritation classification: Category 1

ACTIVITY

Classify a mixture using bridging principles

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MIXTURE 1

MIXTURE 1 Classification for Skin Corrosion/Irritation: Category 1 (based on conclusive data for the whole mixture)

Substance B: Skin Corrosion/Irritation classification: Category 1

MIXTURE 2

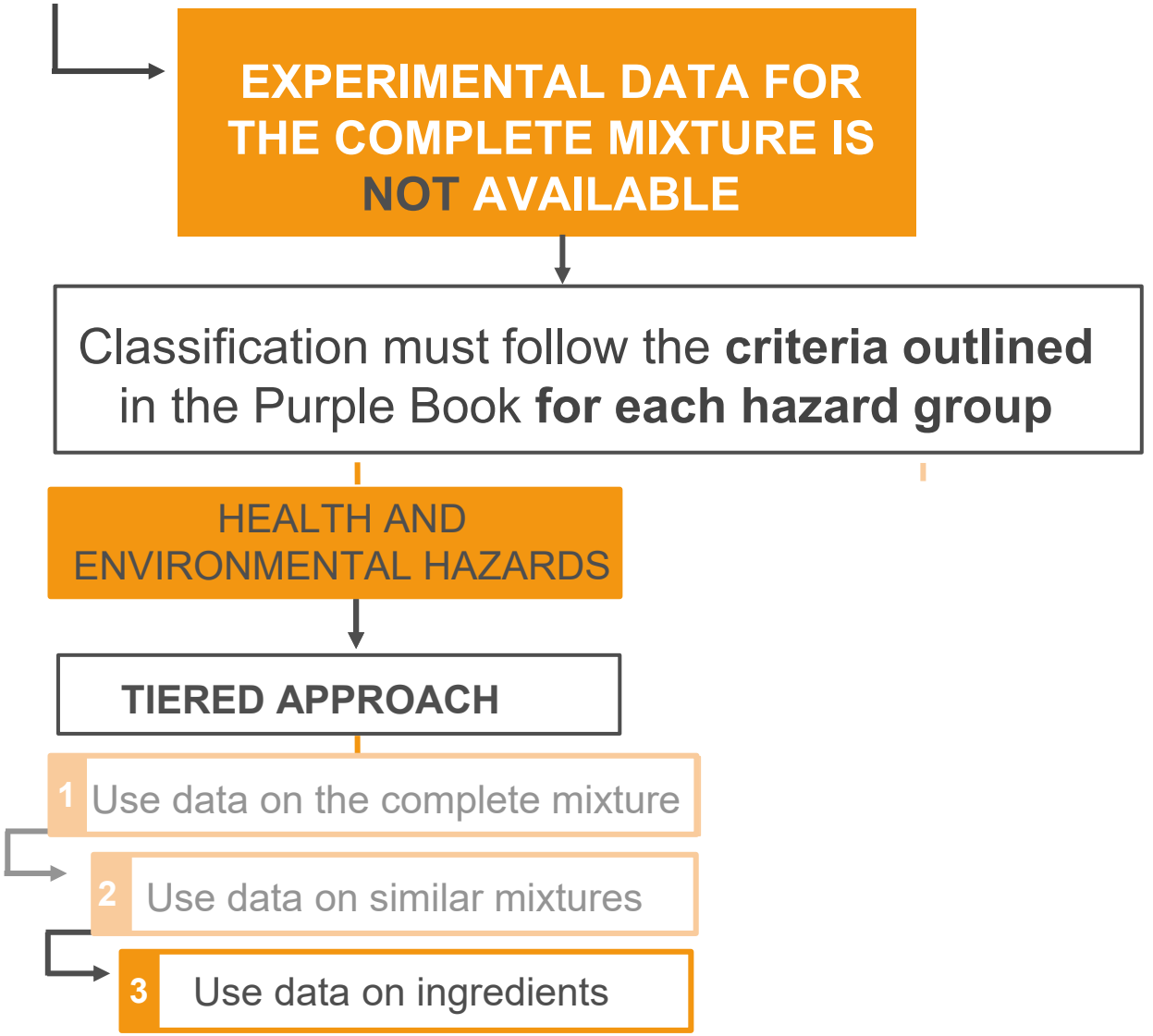
MIXTURE 2 Classification for Skin Corrosion/Irritation:

Category 1

Bridging principle: Substantially similar mixtures

Substance C: Skin Corrosion/Irritation classification: Category 1

What hazard information for the mixture is available?



Classification of mixtures: Health and Environmental hazards

Tiered approach

3 Use available data on ingredients (CUT- OFF VALUES)

- If no data are available for the complete mixture or for similar mixtures, **classification can be based on the hazards of each component of the mixture.**
- Not all ingredients of a mixture contribute equally to its hazardous nature
- To determine which components should be considered **relevant ingredients** for the classification of a mixture, the Purple Book **establishes generic cut-off values**

CUT- OFF VALUE (or concentration limit)

is the threshold at which the presence of a substance must be considered for the classification of a mixture.

3 Use available data on ingredients (CUT- OFF VALUES)

The cut-off/concentration limit is defined for each hazard class in Table 1.5.1 of the Purple Book.

Table 1.5.1: Cut-off values/concentration limits for each health and environmental hazard class

Hazard class	Cut-off value/concentration limit
Acute toxicity	≥ 1.0 %
Skin corrosion/Irritation	≥ 1.0 %
Serious eye damage/eye irritation	≥ 1.0 %
Respiratory/Skin sensitization	≥ 0.1 %
Germ cell mutagenicity (Category 1)	≥ 0.1 %
Germ cell mutagenicity (Category 2)	≥ 1.0 %
Carcinogenicity	≥ 0.1 %
Reproductive toxicity	≥ 0.1 %
Specific target organ toxicity (single exposure)	≥ 1.0 %
Specific target organ toxicity (repeated exposure)	≥ 1.0 %
Aspiration hazard (Category 1)	≥ 1.0 %
Aspiration hazard (Category 2)	≥ 1.0 %
Hazardous to the aquatic environment	≥ 1.0 %

ACTIVITY

Source: Gemini

ACTIVITY

Identify relevant ingredients

- Using Table 1.5.1 of the Purple Book, identify the relevant ingredients of MIXTURE M for:

a) Acute toxicity and
b) Reproductive toxicity

MIXTURE M

INGREDIENT	CONCENTRATION (% W/W)
A	19
B	25
C	0.05
D	0.95
E	55

- Identify the relevant ingredients of MIXTURE M for a) **Acute toxicity** and for b) Reproductive toxicity:

Hazard class	Cut-off value/concentration limit
Acute toxicity	≥ 1.0 %
Skin corrosion/Irritation	≥ 1.0 %
Serious eye damage/eye irritation	≥ 1.0 %
Respiratory/Skin sensitization	≥ 0.1 %
Germ cell mutagenicity (Category 1)	≥ 0.1 %
Germ cell mutagenicity (Category 2)	≥ 1.0 %
Carcinogenicity	≥ 0.1 %
Reproductive toxicity	≥ 0.1 %
Specific target organ toxicity (single exposure)	≥ 1.0 %
Specific target organ toxicity (repeated exposure)	≥ 1.0 %
Aspiration hazard (Category 1)	≥ 1.0 %
Aspiration hazard (Category 2)	≥ 1.0 %
Hazardous to the aquatic environment	≥ 1.0 %

MIXTURE M

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A	19
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- Identify the relevant ingredients of MIXTURE M for a) **Acute toxicity** and for b) Reproductive toxicity:

Hazard class	Cut-off value/concentration limit
Acute toxicity	≥ 1.0 %
Skin corrosion/Irritation	≥ 1.0 %
Serious eye damage/eye irritation	≥ 1.0 %
Respiratory/Skin sensitization	≥ 0.1 %
Germ cell mutagenicity (Category 1)	≥ 0.1 %
Germ cell mutagenicity (Category 2)	≥ 1.0 %
Carcinogenicity	≥ 0.1 %
Reproductive toxicity	≥ 0.1 %
Specific target organ toxicity (single exposure)	≥ 1.0 %
Specific target organ toxicity (repeated exposure)	≥ 1.0 %
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Hazardous to the aquatic environment	≥ 1.0 %

MIXTURE M

INGREDIENT	CONCENTRATION (% W/W)
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Reproductive toxicity	≥ 0.1 %
Specific target organ toxicity (single exposure)	≥ 1.0 %
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Aspiration hazard (Category 2)	≥ 1.0 %
Hazardous to the aquatic environment	≥ 1.0 %

MIXTURE M

INGREDIENT	CONCENTRATION (% W/W)
A	19
B	25
C	0.05
D	0.95
E	55

Classification of mixtures: Health and Environmental hazards

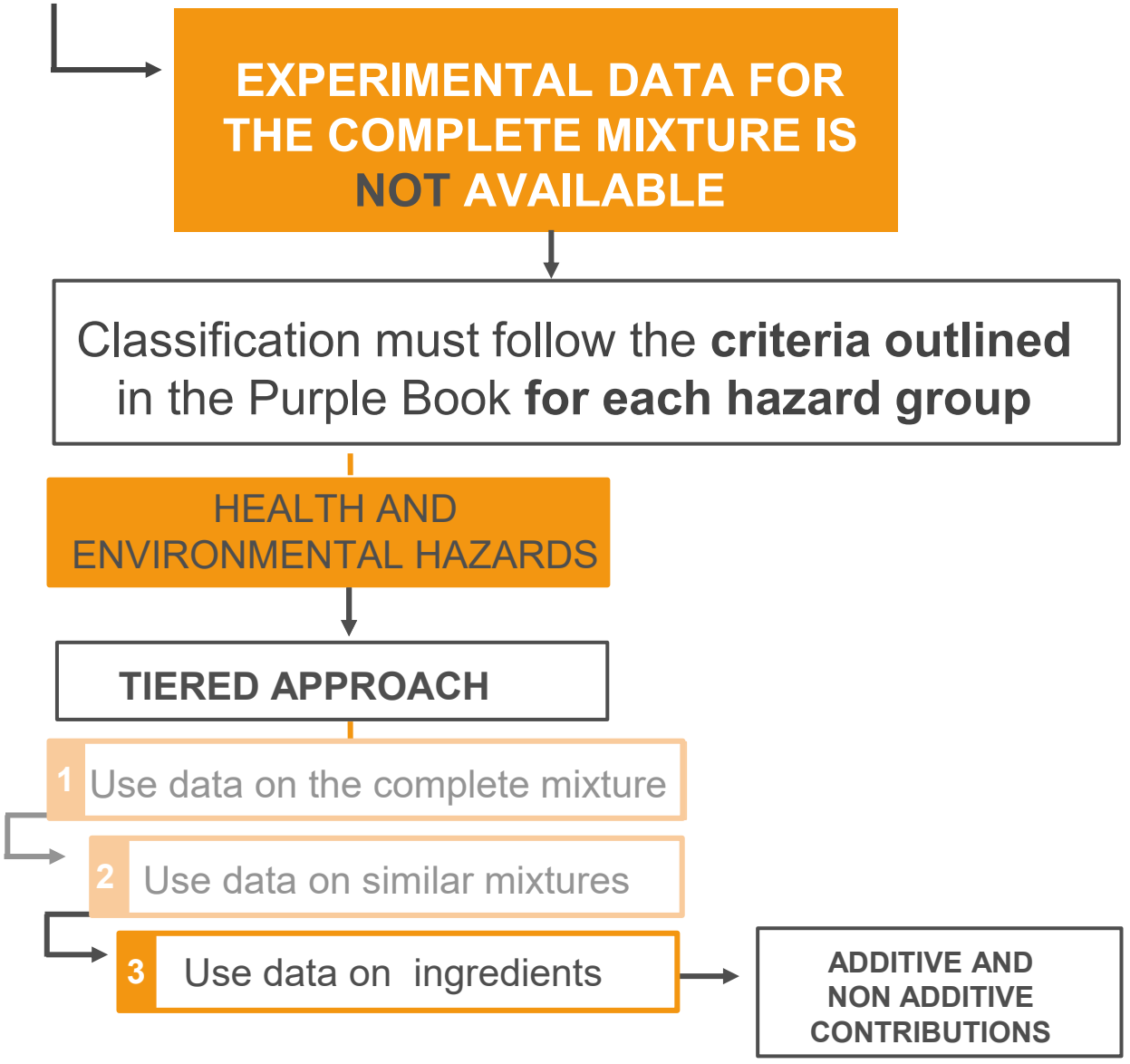
Tiered approach

3 Use available data on ingredients

- Once the relevant ingredients of the mixture for each hazard class have been identified, the classification proceeds according to the specific criteria the Purple Book defines for each hazard class.

- If more than one ingredient is relevant for the same hazard class, the Purple Book established specific classification procedures for the different hazard classes.

What hazard information for the mixture is available?



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Classification of mixtures: Health and Environmental hazards

Tiered approach - Use available data on ingredients

3 Use available data on ingredients

ADDITIVE CONTRIBUTIONS	The hazardous property of the mixture is determined by a weighting of the contributions of the relevant ingredients for that hazard class. This contribution is related to the concentration and toxic potency of each ingredient.	**Hazard classes:** Acute Toxicity, Skin Corrosion/Irritation, Serious Eye Damage/Eye Irritation, Aspiration Hazard, Hazardous to Aquatic Environment, and Specific Target Organ Toxicity only for single exposure when referring to narcotic effects or respiratory irritation.
NON ADDITIVE CONTRIBUTIONS	The mere presence of a hazardous component in the mixture above the concentration limit will determine the classification of the mixture.	**Hazard classes:** Respiratory or Skin Sensitization, Carcinogenicity, Germ Cell Mutagenicity, Reproductive Toxicity, Specific Target Organ Toxicity (single and repeated exposure).

Classification of mixtures: Health and Environmental hazards

Tiered approach - Use available data on ingredients

3 Use available data on ingredients

ADDITIVE CONTRIBUTIONS	The hazardous property of the mixture is determined by a weighting of the contributions of the relevant ingredients for that hazard class. This contribution is related to the concentration and toxic potency of each ingredient.	**Hazard classes:** Acute Toxicity, Skin Corrosion/Irritation, Serious Eye Damage/Eye Irritation, Aspiration Hazard, Hazardous to Aquatic Environment, and Specific Target Organ Toxicity only for single exposure when referring to narcotic effects or respiratory irritation.
NON ADDITIVE CONTRIBUTIONS	The mere presence of a hazardous component in the mixture above the concentration limit will determine the classification of the mixture.	Hazard classes: Respiratory or Skin Sensitization, Carcinogenicity, Germ Cell Mutagenicity, Reproductive Toxicity, Specific Target Organ Toxicity (single and repeated exposure).

Classification of mixtures: Health and Environmental hazards

Tiered approach - Use available data on ingredients - Additive hazards

3 Use available data on ingredients ACUTE TOXICITY

For **acute toxicity,** the Purple Book provides an **additivity formula** to classify mixtures based on their ingredients.

ADDITIVITY FORMULA

weights the contribution of relevant ingredients for a particular hazard.

The additive contribution resulting from an additivity formula is related to the concentration and toxic potency of each ingredient.

Classification of mixtures: Health and Environmental hazards

Tiered approach - Use available data on ingredients - Additive hazards

3 Use available data on ingredients ACUTE TOXICITY

To classify acute toxicity hazards:

- first, identify classified **relevant ingredients** in the mixture;
- then, calculate the **Acute Toxicity Estimate (ATE)** of the mixture **using the additivity formula;**
- finally, use the ATE result to **classify the mixture,** applying the same table used for classifying substances.

ACUTE TOXICITY ESTIMATE (ATE) is a value that indicates an estimation of the acute toxicity of the chemical.

It is derived using LD_{50} (lethal dose 50) or LC_{50} (lethal concentration 50) when available, or other determined criteria if not.

The ATE is specific to each exposure route, so a mixture's ATE must be calculated separately for every route using the relevant data.

unitar course on Classification and labelling available

Classification of mixtures: Health and Environmental hazards

Tiered approach - Use available data on ingredients - Additive hazards

3 Use available data on ingredients ACUTE TOXICITY

A mixture's **Acute Toxicity Estimate (ATE)** is calculated from the ATE values of all relevant ingredients for oral, dermal, and inhalation toxicity using the following **additivity formula:**

$$\frac{100}{\mathrm{ATEmix}} = \sum_{n} \frac{C_i}{\mathrm{ATE}_i}$$

where: Ci = Concentration of the ingredient i;
n ingredients and i is running from 1 to n;
ATEi = Acute toxicity estimate of ingredient i.

3 Use available data on ingredients ACUTE TOXICITY

- Relevant ingredients for this hazard class are those in a concentration equal or above 1% (w/w) in the mixture.

- Ingredients that do not fall into any of the acute toxicity hazard categories are not included in the formula.

Table 1.5.1: Cut-off values/concentration limits for each health and environmental hazard class

Hazard class	Cut-off value/concentration limit
Acute toxicity	≥ 1.0 %
Skin corrosion/Irritation	≥ 1.0 %
Serious eye damage/eye irritation	≥ 1.0 %
Respiratory/Skin sensitization	≥ 0.1 %
Germ cell mutagenicity (Category 1)	≥ 0.1 %
Germ cell mutagenicity (Category 2)	≥ 1.0 %
Carcinogenicity	≥ 0.1 %
Reproductive toxicity	≥ 0.1 %
Specific target organ toxicity (single exposure)	≥ 1.0 %
Specific target organ toxicity (repeated exposure)	≥ 1.0 %

Classification of mixtures: Health and Environmental hazards

Tiered approach - Use available data on ingredients - Additive hazards

3 Use available data on ingredients
ACUTE TOXICITY

- If data on an ingredient is not available but experimental acute toxicity range values or acute hazard categories are known, Table 3.1.2 allows their conversion to acute toxicity point estimates to complete the formula.

Table 3.1.2: Conversion from experimentally obtained acute toxicity range values (or acute toxicity hazard categories) to acute toxicity point estimates for use in the formulas for the classification of mixtures

Exposure routes	Classification category or experimentally obtained acute toxicity range estimate (*see note 1*)	Converted acute toxicity point estimate (*see note 2*)
Oral (mg/kg bodyweight)	0 < Category 1 ≤ 5	0.5
	5 < Category 2 ≤ 50	5
	50 < Category 3 ≤ 300	100
	300 < Category 4 ≤ 2000	500
	2000 < Category 5 ≤ 5000	2500
Dermal (mg/kg bodyweight)	0 < Category 1 ≤ 50	5
	50 < Category 2 ≤ 200	50
	200 < Category 3 ≤ 1000	300
	1000 < Category 4 ≤ 2000	1100
	2000 < Category 5 ≤ 5000	2500
Gases (ppmV)	0 < Category 1 ≤ 100	10
	100 < Category 2 ≤ 500	100
	500 < Category 3 ≤ 2500	700
	2500 < Category 4 ≤ 20000	4500
	Category 5 - See footnote to 3.1.2.5.	
Vapours (mg/l)	0 < Category 1 ≤ 0.5	0.05
	0.5 < Category 2 ≤ 2.0	0.5
	2.0 < Category 3 ≤ 10.0	3
	10.0 < Category 4 ≤ 20.0	11
	Category 5 - See footnote to 3.1.2.5.	
Dust/mist (mg/l)	0 < Category 1 ≤ 0.05	0.005
	0.05 < Category 2 ≤ 0.5	0.05
	0.5 < Category 3 ≤ 1.0	0.5
	1.0 < Category 4 ≤ 5.0	1.5
	Category 5 - See footnote to 3.1.2.5.	

3 Use available data on ingredients ACUTE TOXICITY

1. Identify classified relevant ingredients in the mixture
2. Calculate the ATE for each exposure route

$$\frac{100}{ATEmix} = \sum_{n} \frac{C_i}{ATE_i}$$

3. Use ATE to classify the mixture following Table 3.1.1

Table 3.1.1: Acute toxicity estimate (ATE) values and criteria for acute toxicity hazard categories

Exposure route	Category 1	Category 2	Category 3	Category 4	Category 5
Oral (mg/kg bodyweight) *See notes (a) and (b)*	ATE ≤ 5	5 < ATE ≤ 50	50 < ATE ≤ 300	300 < ATE ≤ 2000	2000< ATE≤ 5000 *See detailed criteria in note (g)*
Dermal (mg/kg bodyweight) *See notes (a) and (b)*	ATE ≤ 50	50 < ATE ≤ 200	200 < ATE ≤ 1000	1000 < ATE ≤ 2000	
Gases (ppmV) *See notes (a), (b) and (c)*	ATE ≤ 100	100 < ATE ≤ 500	500 < ATE ≤ 2500	2500 < ATE ≤ 20000	*See detailed criteria in note (g)*
Vapours (mg/l) *See notes (a), (b), (c), (d) and (e)*	ATE ≤ 0.5	0.5 < ATE ≤ 2.0	2.0 < ATE ≤ 10.0	10.0 < ATE ≤ 20.0	
Dusts and Mists (mg/l) *See notes (a), (b), (c) and (f)*	ATE ≤ 0.05	0.05 < ATE ≤ 0.5	0.5 < ATE ≤ 1.0	1.0 < ATE ≤ 5.0	

EXAMPLE

Mixture (ingredients A+B+C+D) (liquid)

Ingredient		A	B	C	D
Concentration (% w/w)		30	5.5	3.5	61
ATE	oral (mg/Kg body weight)	150	225	30	> 5000
	dermal (mg/kg body weight)	730	130	1100	> 5000
	inhalation (vapours) (mg/L)	> 200	Category 3	6.2	18.0

- Acute toxicity: A, B, C and D are relevant ingredients as their concentrations in the mixture are above the cut-off value for acute toxicity (1%).

EXAMPLE

Mixture (ingredients A+B+C+D) (liquid)

Ingredient		A	B	C	D
Concentration (% w/w)		30	5.5	3.5	61
ATE	oral (mg/Kg body weight)	150	225	30	> 5000

- Oral toxicity: D is not classified as hazardous for the oral route according to Table 3.1.1, for which it is not considered. Calculation includes ingredients A, B and C.

$$\frac{100}{ATEmix} = \frac{30}{150} + \frac{5.5}{225} + \frac{3.5}{30}$$

$$ATEmix\ oral = 293\ mg/kg$$

EXAMPLE

Mixture (ingredients A+B+C+D) (liquid)

Ingredient		A	B	C	D
Concentration (% w/w)		30	5.5	3.5	61
ATE	dermal (mg/kg body weight)	730	130	1100	> 5000

- Dermal toxicity: D is not classified as hazardous for the dermal route, for which it is not considered. Calculation includes ingredients A, B and C.

$$\frac{100}{ATEmix} = \frac{30}{730} + \frac{5.5}{130} + \frac{3.5}{1100}$$

$$\boxed{ATEmix\ dermal = 1155\ mg/kg}$$

EXAMPLE

Mixture (ingredients A+B+C+D) (liquid)

Ingredient		A	B	C	D
Concentration (% w/w)		30	5.5	3.5	61
ATE	inhalation (vapours) (mg/L)	> 200	Category 3	6.2	18.0

- Inhalatory toxicity: A is not classified as hazardous for the inhalation route, for which it is not considered. Calculation includes ingredients B, C and D. Table 3.1.2 is used to obtain the acute toxicity point estimate for ingredient B: as it is classified in category 3 for vapours, the converted value is 3.

$$\frac{100}{ATEmix} = \frac{5.5}{3} + \frac{3.5}{6.2} + \frac{61}{18}$$

$$ATEmix\ vapours = 17.3\ mg/L$$

EXAMPLE

Mixture (ingredients A+B+C+D) (liquid)

- The calculated ATE values are used for the mixture classification according to GHS Table 3.1.1. Each route of exposure has its own classification output.

ATEm oral = 293 mg/kg
ATEm dermal = 1155 mg/kg
ATEm inh (vapours) = 17.3 mg/L

Table 3.1.1: Acute toxicity estimate (ATE) values and criteria for acute toxicity hazard categories

Exposure route	Category 1	Category 2	Category 3	Category 4	Category 5
Oral (mg/kg bodyweight) *See notes (a) and (b)*	ATE ≤ 5	5 < ATE ≤ 50	50 < ATE ≤ 300	300 < ATE ≤ 2000	2000< ATE≤ 5000 *See detailed criteria in note (g)*
Dermal (mg/kg bodyweight) *See notes (a) and (b)*	ATE ≤ 50	50 < ATE ≤ 200	200 < ATE ≤ 1000	1000 < ATE ≤ 2000	
Gases (ppmV) *See notes (a), (b) and (c)*	ATE ≤ 100	100 < ATE ≤ 500	500 < ATE ≤ 2500	2500 < ATE ≤ 20000	*See detailed criteria in note (g)*
Vapours (mg/l) *See notes (a), (b), (c), (d) and (e)*	ATE ≤ 0.5	0.5 < ATE ≤ 2.0	2.0 < ATE ≤ 10.0	10.0 < ATE ≤ 20.0	
Dusts and Mists (mg/l) *See notes (a), (b), (c) and (f)*	ATE ≤ 0.05	0.05 < ATE ≤ 0.5	0.5 < ATE ≤ 1.0	1.0 < ATE ≤ 5.0	

Classification of mixtures: Health and Environmental hazards

Tiered approach - Use available data on ingredients - Additive hazards

3 Use available data on ingredients SKIN CORROSION/ IRRITATION

- The approach to classification of mixtures as corrosive or irritant to skin when data are only available for ingredients, is also based on additivity.

Classification of mixtures: Health and Environmental hazards

Tiered approach - Use available data on ingredients - Additive hazards

3 Use available data on ingredients SKIN CORROSION/ IRRITATION

- A mixture is classified as corrosive/irritant to skin when the sum of the concentrations of the relevant ingredients for a hazard category, exceeds the concentration that triggers classification:

Table 3.2.3: Concentration of ingredients of a mixture classified as skin Category 1, 2 or 3 that would trigger classification of the mixture as hazardous to skin (Category 1, 2 or 3)

Sum of ingredients classified as:	Concentration triggering classification of a mixture as:		
	Skin corrosive	Skin irritant	
	Category 1 (see note below)	Category 2	Category 3
Skin Category 1	≥ 5 %	≥ 1 % but < 5 %	
Skin Category 2		≥ 10 %	≥ 1 % but < 10 %
Skin Category 3			≥ 10 %
(10 × skin Category 1) + skin Category 2		≥ 10 %	≥ 1 % but < 10 %
(10 × skin Category 1) + skin Category 2 + skin Category 3			≥ 10 %

EXAMPLE

Mixture (ingredients A+B+C+D)

Ingredient	A	B	C	D
Concentration (% w/w)	0.05	2.95	95.5	1.5
Skin Corrosion/Irritation classification	Category 2	Category 1	Category 2	Category 1

EXAMPLE

Mixture (ingredients A+B+C+D)

Ingredient	A
Concentration (% w/w)	0.05
Skin Corrosion/Irritation classification	Category 2

Table 1.5.1: Cut-off values/concentration limits for each health and environmental hazard class

Hazard class	Cut-off value/concentration limit
Acute toxicity	≥ 1.0 %
Skin corrosion/Irritation	≥ 1.0 %
Serious eye damage/eye irritation	≥ 1.0 %
Respiratory/Skin sensitization	≥ 0.1 %
Germ cell mutagenicity (Category 1)	≥ 0.1 %
Germ cell mutagenicity (Category 2)	≥ 1.0 %
Carcinogenicity	≥ 0.1 %
Reproductive toxicity	≥ 0.1 %
Specific target organ toxicity (single exposure)	≥ 1.0 %
Specific target organ toxicity (repeated exposure)	≥ 1.0 %
Aspiration hazard (Category 1)	≥ 1.0 %
Aspiration hazard (Category 2)	≥ 1.0 %
Hazardous to the aquatic environment	≥ 1.0 %

EXAMPLE

Mixture (ingredients A+B+C+D)

Ingredient	A	B	C	D
Concentration (% w/w)	0.05	2.95	95.5	1.5
Skin Corrosion/Irritation classification	Category 2	Category 1	Category 2	Category 1

EXAMPLE

Mixture (ingredients A+B+C+D)

Ingredient	A	B	C	D
Concentration (% w/w)	0.05	2.95	95.5	1.5
Skin Corrosion/Irritation classification	Category 2	Category 1	Category 2	Category 1

EXAMPLE

Mixture (ingredients A+B+C+D)

Ingredient	A	B	C	D
Concentration (% w/w)		2.95	+	1.5

=4.45%

Sum of ingredients classified as:	Concentration triggering classification of a mixture as:		
	Skin corrosive	Skin irritant	
	Category 1 (see note below)	Category 2	Category 3
Skin Category 1	≥ 5 %	≥ 1 % but < 5 %	
Skin Category 2		≥ 10 %	≥ 1 % but < 10 %
Skin Category 3			≥ 10 %
(10 × skin Category 1) + skin Category 2		≥ 10 %	≥ 1 % but < 10 %
(10 × skin Category 1) + skin Category 2 + skin Category 3			≥ 10 %

EXAMPLE

Mixture (ingredients A+B+C+D)

Ingredient	A	B	C	D
Concentration (% w/w)		2.95	+	1.5

=4.45%

Sum of ingredients classified as:	Concentration triggering classification of a mixture as:		
	Skin corrosive	Skin irritant	
	Category 1 (see note below)	Category 2	Category 3
Skin Category 1	≥ 5 %	≥ 1 % but < 5 %	
Skin Category 2		≥ 10 %	≥ 1 % but < 10 %
Skin Category 3			≥ 10 %
(10 × skin Category 1) + skin Category 2		≥ 10 %	≥ 1 % but < 10 %
(10 × skin Category 1) + skin Category 2 + skin Category 3			≥ 10 %

EXAMPLE

Mixture (ingredients A+B+C+D)

Ingredient	A	B	C	D
Concentration (% w/w)		2.95	+	1.5

=4.45%

Sum of ingredients classified as:	Concentration triggering classification of a mixture as:		
	Skin corrosive	Skin irritant	
	Category 1 (see note below)	Category 2	Category 3
Skin Category 1	≥ 5 %	≥ 1 % but < 5 %	
Skin Category 2		≥ 10 %	≥ 1 % but < 10 %
Skin Category 3			≥ 10 %
(10 × skin Category 1) + skin Category 2		≥ 10 %	≥ 1 % but < 10 %
(10 × skin Category 1) + skin Category 2 + skin Category 3			≥ 10 %

Classification of mixtures: Health and Environmental hazards

Tiered approach - Use available data on ingredients - Additive hazards

3 Use available data on ingredients HAZARDOUS TO THE AQUATIC ENVIRONMENT

The approach for the classification of aquatic environmental hazards for mixtures includes the **summation of classified ingredients** and/or an **additivity formula**.

SUMMATION METHOD

is used when the classification of the mixture is based on the summation of the concentrations of its classified ingredients.

Classification of mixtures: Health and Environmental hazards

Tiered approach - Use available data on ingredients - Additive hazards

3 Use available data on ingredients HAZARDOUS TO THE AQUATIC ENVIRONMENT

Relevant ingredients are those present in concentrations:

- ≥ 0.1 % (w/w) for ingredients classified as Acute 1 or Chronic 1, and
- ≥ 1 % (w/w) for other ingredients,
- unless very highly toxic ingredients are present (even in concentrations lower than 0.1 % (w/w)).

3 Use available data on ingredients HAZARDOUS TO THE AQUATIC ENVIRONMENT

- The percentage of “Acute” or “Chronic” classified ingredients feeds the GHS Tables 4.1.3 and 4.1.4.

Table 4.1.3: Classification of a mixture for short-term (acute) hazards based on summation of the concentrations of classified ingredients

Sum of the concentrations (in %) of ingredients classified as:		Mixture is classified as:
Acute 1 × M[a]	≥ 25 %	Acute 1
(M × 10 × Acute 1) + Acute 2	≥ 25 %	Acute 2
(M × 100 × Acute 1) + (10 × Acute 2) + Acute 3	≥ 25 %	Acute 3

Table 4.1.4: Classification of a mixture for long-term (chronic) hazards based on summation of the concentrations of classified ingredients

Sum of the concentrations (in %) of ingredients classified as:		Mixture is classified as:
Chronic 1 × M[a]	≥ 25 %	Chronic 1
(M × 10 × Chronic 1) + Chronic 2	≥ 25 %	Chronic 2
(M × 100 × Chronic 1) + (10 × Chronic 2) + Chronic 3	≥ 25 %	Chronic 3
Chronic 1 + Chronic 2 + Chronic 3 + Chronic 4	≥ 25 %	Chronic 4

3 Use available data on ingredients HAZARDOUS TO THE AQUATIC ENVIRONMENT

- When adequate toxicity data are available for more than one ingredient, the combined toxicity of those ingredients may be calculated using an additivity formula.

  - For Acute Aquatic Toxicity:

$$\frac{\Sigma Ci}{L(E)C50m} = \sum_{n} \frac{Ci}{L(E)C50i}$$

where: Ci = Concentration of the ingredient i;
n ingredients and i is running from 1 to n;
L(E)C50i = LC50 or EC50 for ingredient i (in mg/L);
L(E)C50m = LC50 or EC50 for the part of the mixture with test data.

  - For Chronic Aquatic Toxicity:

$$\frac{\Sigma Ci + \Sigma Cj}{EqNOECm} = \sum_{n} \frac{Ci}{NOECi} + \sum_{n} \frac{Cj}{0.1 x NOECj}$$

where: Ci = Concentration of the ingredient i (rapidly degradable ingredients);
Cj = Concentration of the ingredient j (non-rapidly degradable ingredients);
n ingredients and i and j are running from 1 to n;
NOECi = NOEC (or other recognized measures for chronic toxicity) for ingredient i (rapidly degradable ingredients)(in mg/L);
NOECj = NOEC (or other recognized measures for chronic toxicity) for ingredient j (non-rapidly degradable ingredients)(in mg/L);
EqNOECm = Equivalent NOEC of the part of the mixture with test data

Classification of mixtures: Health and Environmental hazards

Tiered approach - Use available data on ingredients - Additive hazards

3 Use available data on ingredients HAZARDOUS TO THE AQUATIC ENVIRONMENT

- When adequate toxicity data are available for more than one ingredient, the combined toxicity of those ingredients may be calculated using an additivity formula.

For Acute Aquatic Toxicity:

$$\frac{\Sigma Ci}{L(E)C50m} = \sum_{n} \frac{Ci}{L(E)C50i}$$

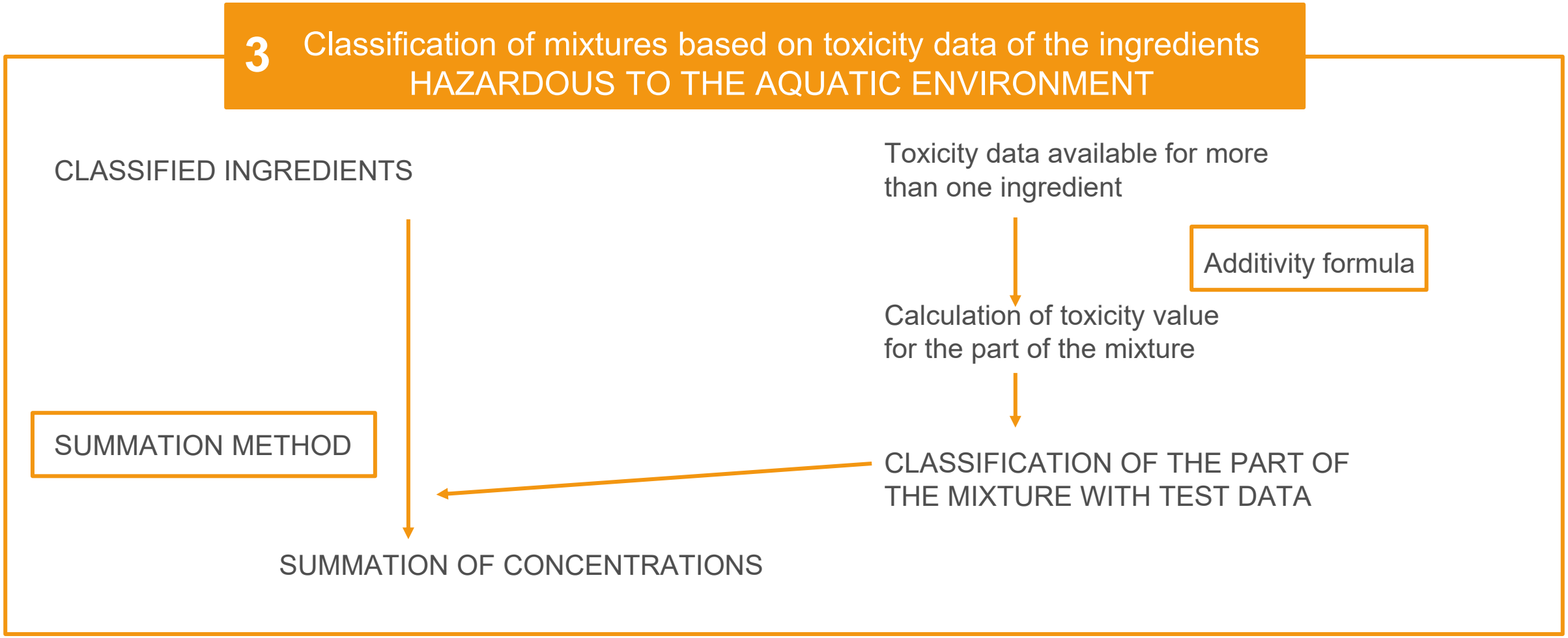
For Chronic Aquatic Toxicity:

$$\frac{\Sigma Ci + \Sigma Cj}{EqNOECm} = \sum_{n} \frac{Ci}{NOECi} + \sum_{n} \frac{Cj}{0.1xNOECj}$$

- The calculated toxicity may be used to assign the portion of the mixture a hazard category which is then used in applying the summation method.

Classification of mixtures: Health and Environmental hazards

Tiered approach - Use available data on ingredients - Additive hazards



EXAMPLE - Summation method

Mixture (ingredients A+B+C) - Chronic Aquatic Toxicity

Ingredient	A	B	C
Concentration (% w/w)	15	75	10
Classification	Chronic 3	Chronic 2	Chronic 2

Classification of mixtures: Health and Environmental hazards

Tiered approach - Use available data on ingredients - Additive hazards

3 Use available data on ingredients HAZARDOUS TO THE AQUATIC ENVIRONMENT

Relevant ingredients are those present in concentrations:

- **≥ 0.1 % (w/w) for ingredients classified as Acute 1 or Chronic 1**, and
- ≥ 1 % (w/w) for other ingredients,
- unless very highly toxic ingredients are present (even in concentrations lower than 0.1 % (w/w)).

EXAMPLE - Summation method

Mixture (ingredients A+B+C) - Chronic Aquatic Toxicity

Ingredient	A	B	C
Concentration (% w/w)	15	75	10
Classification	Chronic 3	Chronic 2	Chronic 2

EXAMPLE - Summation method

Mixture (ingredients A+B+C) - Chronic Aquatic Toxicity

Table 4.1.4: Classification of a mixture for long-term (chronic) hazards based on summation of the concentrations of classified ingredients

Sum of the concentrations (in %) of ingredients classified as:		Mixture is classified as:
Chronic 1 × M[a]	≥ 25 %	Chronic 1
(M × 10 × Chronic 1) + Chronic 2	≥ 25 %	Chronic 2
(M × 100 × Chronic 1) + (10 × Chronic 2) + Chronic 3	≥ 25 %	Chronic 3
Chronic 1 + Chronic 2 + Chronic 3 + Chronic 4	≥ 25 %	Chronic 4

EXAMPLE - Summation method

Mixture (ingredients A+B+C) - Chronic Aquatic Toxicity

Ingredient	A	B	C
Concentration (% w/w)	15	75	10
Classification	Chronic 3	Chronic 2	Chronic 2

EXAMPLE - Summation method

Mixture (ingredients A+B+C) - Chronic Aquatic Toxicity

Table 4.1.4: Classification of a mixture for long-term (chronic) hazards based on summation of the concentrations of classified ingredients

Sum of the concentrations (in %) of ingredients classified as:		Mixture is classified as:
Chronic 1 × M[a]	≥ 25 %	Chronic 1
(M × 10 × Chronic 1) + Chronic 2	≥ 25 %	Chronic 2
(M × 100 × Chronic 1) + (10 × Chronic 2) + Chronic 3	≥ 25 %	Chronic 3
Chronic 1 + Chronic 2 + Chronic 3 + Chronic 4	≥ 25 %	Chronic 4

EXAMPLE - Summation method

Mixture (ingredients A+B+C) - Chronic Aquatic Toxicity

Ingredient	A	B		C
Concentration (% w/w)		75	+	10 = 85%
Classification	Chronic 3	Chronic 2		Chronic 2

EXAMPLE - Summation method

Mixture (ingredients A+B+C) - Chronic Aquatic Toxicity

Table 4.1.4: Classification of a mixture for long-term (chronic) hazards based on summation of the concentrations of classified ingredients

Sum of the concentrations (in %) of ingredients classified as:		Mixture is classified as:
Chronic 1 × M[a]	≥ 25 %	Chronic 1
(M × 10 × Chronic 1) + Chronic 2	≥ 25 %	Chronic 2
(M × 100 × Chronic 1) + (10 × Chronic 2) + Chronic 3	≥ 25 %	Chronic 3
Chronic 1 + Chronic 2 + Chronic 3 + Chronic 4	≥ 25 %	Chronic 4

= 85%

Classification of mixtures: Health and Environmental hazards

Very highly toxic ingredients

3 Use available data on ingredients
HAZARDOUS TO THE AQUATIC ENVIRONMENT

For **Very highly toxic ingredients** classified as Acute 1 or Chronic 1, attention should be paid to those with:

- acute toxicity below 1 mg/L and/or
- chronic toxicity below 0,1 mg/L (if not rapidly degradable)
- or 0.01 mg/L (if rapidly degradable).

These **contribute to the toxicity of the mixture even in concentrations below the cut-off values** for the hazard class.

3 Use available data on ingredients HAZARDOUS TO THE AQUATIC ENVIRONMENT

- Multiplying factors for these ingredients are needed to avoid under classification of the mixture.

Table 4.1.5: Multiplying factors for highly toxic ingredients of mixtures

Acute toxicity	M factor	Chronic toxicity	M factor	
$L(E)C_{50}$ value		NOEC value	NRD[a] ingredients	RD[b] ingredients
$0.1 < L(E)C_{50} \leq 1$	1	$0.01 < NOEC \leq 0.1$	1	-
$0.01 < L(E)C_{50} \leq 0.1$	10	$0.001 < NOEC \leq 0.01$	10	1
$0.001 < L(E)C_{50} \leq 0.01$	100	$0.0001 < NOEC \leq 0.001$	100	10
$0.0001 < L(E)C_{50} \leq 0.001$	1000	$0.00001 < NOEC \leq 0.0001$	1000	100
$0.00001 < L(E)C_{50} \leq 0.0001$	10000	$0.000001 < NOEC \leq 0.00001$	10000	1000
(continue in factor 10 intervals)		(continue in factor 10 intervals)		

[a] *Non-rapidly degradable*
[b] *Rapidly degratdable*

3 Use available data on ingredients HAZARDOUS TO THE AQUATIC ENVIRONMENT

- M factors for Acute and Chronic Toxicity are defined by the toxicity values of ingredients as shown in GHS Table 4.1.5.

Table 4.1.5: Multiplying factors for highly toxic ingredients of mixtures

Acute toxicity	M factor	Chronic toxicity	M factor	
$L(E)C_{50}$ value		NOEC value	NRD[a] ingredients	RD[b] ingredients
$0.1 < L(E)C_{50} \leq 1$	1	$0.01 < NOEC \leq 0.1$	1	-
$0.01 < L(E)C_{50} \leq 0.1$	10	$0.001 < NOEC \leq 0.01$	10	1
$0.001 < L(E)C_{50} \leq 0.01$	100	$0.0001 < NOEC \leq 0.001$	100	10
$0.0001 < L(E)C_{50} \leq 0.001$	1000	$0.00001 < NOEC \leq 0.0001$	1000	100
$0.00001 < L(E)C_{50} \leq 0.0001$	10000	$0.000001 < NOEC \leq 0.00001$	10000	1000
(continue in factor 10 intervals)		(continue in factor 10 intervals)		

[a] *Non-rapidly degradable*
[b] *Rapidly degratdable*

EXAMPLE - Summation method + additivity formula

Mixture (ingredients A+B+C+D) - Acute Aquatic Toxicity

Ingredient	A	B	C	D
Concentration (% w/w)	25	65	9.5	0.5
Classification	-	-	Acute 2	Acute 1
LC50 96h fish (mg/L)	6.7	26.8	-	-
M factor	-	-	-	10

EXAMPLE - Summation method + additivity formula

Mixture (ingredients A+B+C+D) - Acute Aquatic Toxicity

Ingredient	A	B	C	D
Concentration (% w/w)	25	65	9.5	0.5 **> 0.1%**
Classification	-	-	Acute 2	Acute 1
LC50 96h fish (mg/L)	6.7	26.8	-	-
M factor	-	-	-	10

EXAMPLE - Summation method + additivity formula

Mixture (ingredients A+B+C+D) - Acute Aquatic Toxicity

Ingredient	A	B	C	D
Concentration (% w/w)	25	65	9.5	0.5
Classification	-	-	Acute 2	Acute 1
LC50 96h fish (mg/L)	6.7	26.8	-	-
M factor	-	-	-	10

EXAMPLE - Summation method + additivity formula

Mixture (ingredients A+B+C+D) - Acute Aquatic Toxicity

- Using of the additivity formula:

$$\frac{\Sigma Ci}{L(E)C50m} = \sum_{n} \frac{Ci}{L(E)C50i}$$

where: Ci = Concentration of the ingredient i;
n ingredients and i is running from 1 to n;
L(E)C50i = LC50 or EC50 for ingredient i (in mg/L);
L(E)C50m = LC50 or EC50 for the part of the mixture with test data.

- For ingredients A and B in the mixture, the result is:

$$\frac{(25+65)}{LC50m} = \frac{25}{6.7} + \frac{65}{26.8}$$

$$\boxed{LC50m\ (fish) = 14.6\ mg/L}$$

EXAMPLE - Summation method + additivity formula

Mixture (ingredients A+B+C+D) - Acute Aquatic Toxicity

- For ingredients A and B in the mixture, the result is: $LC50m\ (fish) = 14.6\ mg/L$

Table 4.1.1: Categories for substances hazardous to the aquatic environment *(Note 1)*

(a) Short-term (acute) aquatic hazard

Category Acute 1: *(Note 2)*	
96 hr LC_{50} (for fish)	≤ 1 mg/l and/or
48 hr EC_{50} (for crustacea)	≤ 1 mg/l and/or
72 or 96hr ErC_{50} (for algae or other aquatic plants)	≤ 1 mg/l *(Note 3)*
Category Acute 1 may be subdivided for some regulatory systems to include a lower band at $L(E)C_{50}$ ≤ 0.1 mg/l	
Category Acute 2:	
96 hr LC_{50} (for fish)	> 1 but ≤ 10 mg/l and/or
48 hr EC_{50} (for crustacea)	> 1 but ≤ 10 mg/l and/or
72 or 96hr ErC_{50} (for algae or other aquatic plants)	> 1 but ≤ 10 mg/l *(Note 3)*
Category Acute 3:	
96 hr LC_{50} (for fish)	> 10 but ≤ 100 mg/l and/or
48 hr EC_{50} (for crustacea)	> 10 but ≤ 100 mg/l and/or
72 or 96hr ErC_{50} (for algae or other aquatic plants)	> 10 but ≤ 100 mg/l *(Note 3)*
Some regulatory systems may extend this range beyond an $L(E)C_{50}$ of 100 mg/l through the introduction of another category.	

14.6mg/L

EXAMPLE - Summation method + additivity formula

Mixture (ingredients A+B+C+D) - Acute Aquatic Toxicity

Ingredient	A	B	C	D
Concentration (% w/w)	25	65	9.5	0.5
Classification	Acute 3		Acute 2	Acute 1
LC50 96h fish (mg/L)	6.7	26.8	-	-
M factor	-	-	-	10

EXAMPLE - Summation method + additivity formula

Mixture (ingredients A+B+C+D) - Acute Aquatic Toxicity

- The summation method is applied according to GHS Table 4.1.3

Table 4.1.3: Classification of a mixture for short-term (acute) hazards based on summation of the concentrations of classified ingredients

Sum of the concentrations (in %) of ingredients classified as:		Mixture is classified as:
Acute 1 × M[a]	≥ 25 %	Acute 1
(M × 10 × Acute 1) + Acute 2	≥ 25 %	Acute 2
(M × 100 × Acute 1) + (10 × Acute 2) + Acute 3	≥ 25 %	Acute 3

EXAMPLE - Summation method + additivity formula

Mixture (ingredients A+B+C+D) - Acute Aquatic Toxicity

Ingredient	A	B	C	D
Concentration (% w/w)	25	65	9.5	0.5
Classification	Acute 3		Acute 2	Acute 1
LC50 96h fish (mg/L)	6.7	26.8	-	-
M factor	-	-	-	10

EXAMPLE - Summation method + additivity formula

Mixture (ingredients A+B+C+D) - Acute Aquatic Toxicity

- The summation method is applied according to GHS Table 4.1.3

Table 4.1.3: Classification of a mixture for short-term (acute) hazards based on summation of the concentrations of classified ingredients

Sum of the concentrations (in %) of ingredients classified as:		Mixture is classified as:
Acute 1 × M[a] ⟶ 0.5 x 10 = 5	≥ 25 %	Acute 1
(M × 10 × Acute 1) + Acute 2	≥ 25 %	Acute 2
(M × 100 × Acute 1) + (10 × Acute 2) + Acute 3	≥ 25 %	Acute 3

EXAMPLE - Summation method + additivity formula

Mixture (ingredients A+B+C+D) - Acute Aquatic Toxicity

- The summation method is applied according to GHS Table 4.1.3

Table 4.1.3: Classification of a mixture for short-term (acute) hazards based on summation of the concentrations of classified ingredients

Sum of the concentrations (in %) of ingredients classified as:		Mixture is classified as:
Acute 1 × M[a] ⟶ 0.5 x 10 = 5 < 25%	≥ 25 %	Acute 1
(M × 10 × Acute 1) + Acute 2	≥ 25 %	Acute 2
(M × 100 × Acute 1) + (10 × Acute 2) + Acute 3	≥ 25 %	Acute 3

EXAMPLE - Summation method + additivity formula

Mixture (ingredients A+B+C+D) - Acute Aquatic Toxicity

- The summation method is applied according to GHS Table 4.1.3

Table 4.1.3: Classification of a mixture for short-term (acute) hazards based on summation of the concentrations of classified ingredients

Sum of the concentrations (in %) of ingredients classified as:		Mixture is classified as:
Acute 1 × M[a]	≥ 25 %	Acute 1
(M × 10 × Acute 1) + Acute 2	≥ 25 %	Acute 2
(M × 100 × Acute 1) + (10 × Acute 2) + Acute 3	≥ 25 %	Acute 3

EXAMPLE - Summation method + additivity formula

Mixture (ingredients A+B+C+D) - Acute Aquatic Toxicity

Ingredient	A	B	C	D
Concentration (% w/w)	25	65	9.5	0.5
Classification	Acute 3		Acute 2	Acute 1
LC50 96h fish (mg/L)	6.7	26.8	-	-
M factor	-	-	-	10

EXAMPLE - Summation method + additivity formula

Mixture (ingredients A+B+C+D) - Acute Aquatic Toxicity

- The summation method is applied according to GHS Table 4.1.3

Table 4.1.3: Classification of a mixture for short-term (acute) hazards based on summation of the concentrations of classified ingredients

Sum of the concentrations (in %) of ingredients classified as:		Mixture is classified as:
Acute 1 × M[a]	≥ 25 %	Acute 1
(M × 10 × Acute 1) + Acute 2	≥ 25 %	Acute 2
(M × 100 × Acute 1) + (10 × Acute 2) + Acute 3	≥ 25 %	Acute 3

(10 x 10 x 0.5) + 9.5 = 59.5

EXAMPLE - Summation method + additivity formula

Mixture (ingredients A+B+C+D) - Acute Aquatic Toxicity

- The summation method is applied according to GHS Table 4.1.3

Table 4.1.3: Classification of a mixture for short-term (acute) hazards based on summation of the concentrations of classified ingredients

Sum of the concentrations (in %) of ingredients classified as:		Mixture is classified as:
Acute 1 × M[a]	≥ 25 %	Acute 1
(M × 10 × Acute 1) + Acute 2	≥ 25 %	Acute 2
(M × 100 × Acute 1) + (10 × Acute 2) + Acute 3	≥ 25 %	Acute 3

(10 x 10 x 0.5) + 9.5 = 59.5 ≥ 25%

ACTIVITY

Source: Gemini

ACTIVITY

Classify a mixture using available data for the individual ingredients. Additive hazards

Classify MIXTURE Y using data for the individual ingredients and composition, for **oral and dermal Acute Toxicity** (Additivity formula and Table 3.1.1) and **Serious Eye Damage/Eye Irritation** (Table 3.3.3).

Ingredient	**A**	**B**	**C**	**D**
Concentration (% w/w)	15	15	0,05	69,95
LD50 oral (mg/kg)	1650	1800	350	> 5000
LD50 dermal (mg/kg)	35	250	1500	> 5000
Serious Eye Damage/Eye Irritation classification	Category 2A	Not classified	Category 2A	Not classified

ACTIVITY

Classify a mixture using available data for the individual ingredients. Additive hazards

- Classify MIXTURE Y using data for the individual ingredients and composition, for oral and dermal Acute toxicity and Serious Eye Damage/Eye Irritation.

Hazard class	**Classification**
Acute toxicity oral	Not classified
Acute toxicity dermal	Category 3
Serious Eye Damage/Eye Irritation	Category 2/2A

ACTIVITY

Classify a mixture using available data for the individual ingredients. Additive hazards

Table 3.3.3: Concentration of ingredients of a mixture classified as skin Category 1 and/or eye Category 1 or 2 that would trigger classification of the mixture as hazardous to the eye (Category 1 or 2)

Sum of ingredients classified as	Concentration triggering classification of a mixture as:	
	serious eye damage	eye irritation
	Category 1	Category 2/2A
Skin Category 1 + eye Category 1[a]	≥ 3 %	≥ 1 % but < 3 %
Eye Category 2		≥ 10 %[b]
10 × (skin Category 1 + eye Category 1)[a] + eye Category 2		≥ 10 %

[a] *If an ingredient is classified as both skin Category 1 and eye Category 1 its concentration is considered only once in the calculation;*

[b] *A mixture may be classified as eye Category 2B when all relevant ingredients are classified as eye Category 2B.*

Classification of mixtures: Health and Environmental hazards

Tiered approach - Use available data on ingredients - Non Additive hazards

3 Use available data on ingredients

ADDITIVE CONTRIBUTIONS	The hazardous property of the mixture is determined by a weighting of the contributions of the relevant ingredients for that hazard class. This contribution is related to the concentration and toxic potency of each ingredient.	Hazard classes: Acute Toxicity, Skin Corrosion/Irritation, Serious Eye Damage/Eye Irritation, Aspiration Hazard, Hazardous to Aquatic Environment, and Specific Target Organ Toxicity only for single exposure when referring to narcotic effects or respiratory irritation.
NON ADDITIVE CONTRIBUTIONS	The mere presence of a hazardous component in the mixture above the concentration limit will determine the classification of the mixture.	Hazard classes: Respiratory or Skin Sensitization, Carcinogenicity, Germ Cell Mutagenicity, Reproductive Toxicity, Specific Target Organ Toxicity (single and repeated exposure).

EXAMPLE

Mixture (ingredients A+B+C) - Non additive hazards - Carcinogenicity

Ingredient	**A**	**B**	**C**
Concentration (% w/w)	15.5	75	0.5
Carcinogenicity Classification	Not classified	Not classified	1A

EXAMPLE

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Mixture (ingredients A+B+C) - Non additive hazards - Carcinogenicity

Table 1.5.1: Cut-off values/concentration limits for each health and environmental hazard class

Hazard class	Cut-off value/concentration limit
Acute toxicity	≥ 1.0 %
Skin corrosion/Irritation	≥ 1.0 %
Serious eye damage/eye irritation	≥ 1.0 %
Respiratory/Skin sensitization	≥ 0.1 %
Germ cell mutagenicity (Category 1)	≥ 0.1 %
Germ cell mutagenicity (Category 2)	≥ 1.0 %
Carcinogenicity	≥ 0.1 %
Reproductive toxicity	≥ 0.1 %
Specific target organ toxicity (single exposure)	≥ 1.0 %
Specific target organ toxicity (repeated exposure)	≥ 1.0 %
Aspiration hazard (Category 1)	≥ 1.0 %
Aspiration hazard (Category 2)	≥ 1.0 %
Hazardous to the aquatic environment	≥ 1.0 %

EXAMPLE

Mixture (ingredients A+B+C) - Non additive hazards - Carcinogenicity

Ingredient	**A**	**B**	**C**
Concentration (% w/w)	15.5	75	0.5
Carcinogenicity Classification	Not classified	Not classified	1A

EXAMPLE

Mixture (ingredients A+B+C) - Non additive hazards - Carcinogenicity

Table 3.6.1: Cut-off values/concentration limits of ingredients of a mixture classified as carcinogen that would trigger classification of the mixture [a]

Ingredient classified as:	Cut-off/concentration limits triggering classification of a mixture as:		
	Category 1 carcinogen		Category 2 carcinogen
	Category 1A	Category 1B	
Category 1A carcinogen	≥ 0.1 %	--	--
Category 1B carcinogen	--	≥ 0.1 %	
Category 2 carcinogen	--	--	≥ 0.1 % (note 1)
			≥ 1.0 % (note 2)

EXAMPLE

Mixture (ingredients A+B+C) - Non additive hazards - Carcinogenicity

Ingredient	**A**	**B**	**C**
Concentration (% w/w)	15.5	75	0.5
Carcinogenicity Classification	Not classified	Not classified	1A

EXAMPLE

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Mixture (ingredients A+B+C) - Non additive hazards - Respiratory or Skin Sensitization

Ingredient	**A**	**B**	**C**
Concentration (% w/w)	99.80	0.15	0.05
Respiratory Sensitization Classification	Not classified	Respiratory Sensitization 1A	Skin Sensitization 1A

EXAMPLE

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Mixture (ingredients A+B+C) - Non additive hazards - Respiratory or Skin Sensitization

Table 1.5.1: Cut-off values/concentration limits for each health and environmental hazard class

Hazard class	Cut-off value/concentration limit
Acute toxicity	≥ 1.0 %
Skin corrosion/Irritation	≥ 1.0 %
Serious eye damage/eye irritation	≥ 1.0 %
Respiratory/Skin sensitization	≥ 0.1 %
Germ cell mutagenicity (Category 1)	≥ 0.1 %
Germ cell mutagenicity (Category 2)	≥ 1.0 %
Carcinogenicity	≥ 0.1 %
Reproductive toxicity	≥ 0.1 %
Specific target organ toxicity (single exposure)	≥ 1.0 %
Specific target organ toxicity (repeated exposure)	≥ 1.0 %
Aspiration hazard (Category 1)	≥ 1.0 %
Aspiration hazard (Category 2)	≥ 1.0 %
Hazardous to the aquatic environment	≥ 1.0 %

EXAMPLE

Mixture (ingredients A+B+C) - Non additive hazards - Respiratory or Skin Sensitization

Ingredient	**A**	**B**	**C**
Concentration (% w/w)	99.80	0.15	0.05
Respiratory Sensitization Classification	Not classified	Respiratory Sensitization 1A	Skin Sensitization 1A

EXAMPLE

Mixture (ingredients A+B+C) - Non additive hazards - Respiratory or Skin Sensitization

Ingredient	**A**	**B**	**C**
Concentration (% w/w)	99.80	0.15	0.05
Respiratory Sensitization Classification	Not classified	Respiratory Sensitization 1A	Skin Sensitization 1A

EXAMPLE

Mixture (ingredients A+B+C) - Non additive hazards - Respiratory or Skin Sensitization

Ingredient	**A**	**B**	**C**
Concentration (% w/w)	99.80	0.15	0.05
Respiratory Sensitization Classification	Not classified	Respiratory Sensitization 1A	Skin Sensitization 1A

EXAMPLE

Mixture (ingredients A+B+C) - Non additive hazards - Respiratory Sensitization

Table 3.4.5: Cut-off values/concentration limits of ingredients of a mixture classified as either respiratory sensitizers or skin sensitizers that would trigger classification of the mixture

Ingredient classified as:	Cut-off values/concentration limits triggering classification of a mixture as:		
	respiratory sensitizer Category 1		skin sensitizer Category 1
	Solid/Liquid	Gas	All physical states
Respiratory sensitizer Category 1	≥ 0.1 % (see note)	≥ 0.1 % (see note)	--
	≥ 1.0 %	≥ 0.2 %	
Respiratory sensitizer sub-category 1A	≥ 0.1 %	≥ 0.1 %	
Respiratory sensitizer sub-category 1B	≥ 1.0 %	≥ 0.2 %	
Skin sensitizer Category 1	--		
	--		
Skin sensitizer sub-category 1A	--		
Skin sensitizer sub-category 1B	--	--	≥ 1.0 %

Ingredient B = 0.15% ≥ 0.1%

ACTIVITY

Source: Gemini

ACTIVITY

Classify MIXTURE X - Available data for the individual ingredients. Non-additive hazards

Ingredient	A	B	C	D
Concentration	0.05	2.8	0.15	97
Carcinogenicity classification	Not classified	Not classified	Category 1A	Not classified
Germ Cell Mutagenicity classification	Category 1B	Not classified	Category 1B	Not classified
Specific Target Organ Toxicity - Repeated exposure classification	Category 1	Not classified	Not classified	Not classified

ACTIVITY

Classify MIXTURE X - Available data for the individual ingredients. Non-additive hazards

Hazard class	Classification
Carcinogenicity	
Germ Cell Mutagenicity	
Specific Target Organ Toxicity - Repeated exposure	

ACTIVITY

Classify MIXTURE X - Available data for the individual ingredients. Non-additive hazards

Hazard class	Classification
Carcinogenicity	Category 1A
Germ Cell Mutagenicity	Category 1B
Specific Target Organ Toxicity - Repeated exposure	Not classified

KICK OFF QUESTIONS: LET'S REVIEW

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Thank You!

We hope you enjoyed the presentation

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