United Nations ST/SG/AC.10/C.4/2010/15

Secretariat

Distr.: General
22 September 2010

Original: English

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

Twentieth session
Geneva, 7–9 December 2010
Item 4 (a) of the provisional agenda
Implementation of the GHS – Implementation issues

Proposals to address issues from the programme of work for the practical classification issues correspondence group

Transmitted by the expert from the United States of America on behalf of the informal correspondence group on practical classification issues[1]

Purpose

1. By way of this document, the informal correspondence working group on practical classification issues is providing recommendations to clarify classification criteria in the GHS and worked examples on applying GHS criteria.

Background

2. At its seventeenth session, the Sub-Committee approved the programme of work to be undertaken by the practical classification issues informal correspondence group for the current biennium (see INF.5 submitted at the seventeenth session). Many of the work items were drawn from the document submitted by the implementation informal working group in December 2008 (see ST/SG/AC.10/C.4/2008/22).

3. This document is the culmination of the work that has been conducted over the past two years, beginning at the sixteenth session of the Sub-Committee in December 2008. During the course of this two-year period, the informal correspondence group has taken the

[1] In accordance with the programme of work of the Sub-Committee for 2009-2010 approved by the Committee at its fourth session (refer to ST/SG/AC.10/C.4/32, Annex II and ST/SG/AC.10/36, para.14).

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approach of creating thought starter papers to describe the issues on its programme of work in detail and suggest alternate approaches to clarifying the GHS text. The thought starter papers also presented draft worked examples illustrating the application of the bridging principle and hazards to the aquatic environment criteria. The thought starters provided the informal working group the opportunity to discuss the advantages and disadvantages of alternate approaches to editorial revisions and the worked examples. The results of these discussions provided the basis for the group to reach a consensus path forward on the proposed editorial changes to the GHS text and worked examples.

4. The solutions that the correspondence group is proposing fall into three categories:

(a) Editorial revisions to the GHS text (see annex 1);

(b) Worked examples demonstrating the application of bridging principles to mixtures (see annex 2); and

(c) Worked examples demonstrating the application of the classification criteria for mixtures hazardous to the aquatic environment (see annex 3).

Proposal

5. The correspondence group requests that the Sub-Committee approve:

(a) The recommended editorial changes to the GHS text. These approved changes would be incorporated into the next revised edition of the GHS;

(b) The worked examples demonstrating application of the GHS bridging principles to mixtures and the classification criteria for mixtures hazardous to the aquatic environment. These worked examples would then be proposed for inclusion in the training document which is being developed by the United Nations Institute for Training and Research (UNITAR).

6. This document and these recommendations are put before the Sub-Committee for consideration and approval.

Annex 1

Proposed editorial amendments to the GHS text

Chapter 1.3: Classification of hazardous substances and mixtures

(see INF.24 (19th session), Annex 1, Item 1)

1.3.2.3 Insert "1.3.2.3.1" before the first paragraph ("The classification criteria….") and amend the beginning of the second sentence to read: "For most hazard classes, the recommended process….".

1.3.2.3.2 Insert a new paragraph 1.3.2.3.2 as follows:

"1.3.2.3.2 In most cases, it is not anticipated that reliable data for complete mixtures will be available for germ cell mutagenicity, carcinogenicity, and reproductive toxicity hazard classes. Therefore, for these hazard classes, mixtures will generally be classified based on the available information for the individual ingredients of the mixtures, using the cut-off values/concentration limit methods in each chapter. The classification may be modified on a case-by-case basis based on available test data for the complete mixture, if such data are conclusive as described in each chapter."

Chapter 3.1: Acute toxicity

(see INF.24 (19th session), Annex 1, Items 2 and 4)

3.1.3.6.2.2 At the end of the second sentence, replace "unknown toxicity" with "unknown acute (oral/dermal/inhalation) toxicity".

Add the following new third sentence at the end of the existing text:

"The competent authority can decide to specify that the additional statement(s) be communicated on the label or on the SDS or both, or to leave the choice of where to place the statement to the manufacturer/supplier."

3.1.3.6.2.3 Insert "relevant" before "ingredient(s)" (twice) and delete "total" before "percentage".

3.1.4 Insert "3.1.4.1" before the first paragraph ("General and specific considerations….").

3.1.4.2 Insert a new paragraph 3.1.4.2 after the Note to Table 3.1.3 to read as follows:

"3.1.4.2 The acute toxicity hazard statements differentiate the hazard based on the route of exposure. Communication of Acute Toxicity classification should also reflect this differentiation. For example, acute oral toxicity Category 1, acute dermal toxicity Category 1 and acute inhalation toxicity Category 1. If a substance or mixture is classified for more than one route of exposure then all relevant classifications should be communicated on the safety data sheet as specified in Annex 4 and the relevant hazard communication elements included on the label as prescribed in 3.1.3.2. If the statement "x percent of the mixture consists of ingredient(s) of unknown acute (oral/dermal/inhalation) toxicity" is communicated, as prescribed in paragraph 3.1.3.6.2.2, then it can also be differentiated based on the route of exposure. For example, "x percent of the mixture consists of ingredient(s) of

unknown acute oral toxicity" and "x percent of the mixture consists of ingredient(s) of unknown acute dermal toxicity."

3.1.5.2 Amend footnote 3 to the decision logic to read as follows *(changes are indicated):*

"In the event that an ingredient without any useable information is used in a mixture at a concentration ≥1%, the classification should be based on the ingredients with the known acute toxicity only, and additional statement(s) should identify the fact that ~~the~~ x percent of the mixture consists of ingredient(s) of unknown acute (oral/dermal/inhalation) toxicity. ~~of x % of the mixture is unknown.~~ The competent authority can decide to specify that the additional statement(s) be communicated on the label or on the SDS or both, or to leave the choice of where to place the statement to the manufacturer/supplier."

Annex 4: Guidance on the preparation of Safety Data Sheets (SDS)

(see INF.24 (19th session), Annex I, Item 2)

A4.3.2.1.2 Amend as follows (changes are indicated):

"If the substance or mixture is classified in accordance with Parts 2, 3 and/or 4 of the GHS generally the classification is communicated by providing the appropriate hazard class and category to indicate the hazard. For example, flammable liquid Category 1. However, when classification is differentiated within a hazard class and results in unique hazard statements, then the classification should also reflect that differentiation. For example, the route of exposure differentiates the Acute Toxicity classification as follows: acute oral toxicity Category 1, acute dermal toxicity Category 1 and acute inhalation toxicity Category 1. If a substance or mixture is classified into more than one category in a hazard class that is differentiated, then all classifications should be communicated."

Chapter 3.5: Germ cell mutagenicity

(see INF.24 (19th session), Annex 1, Item 5)

3.5.3.3 Amend Table 3.5.1 to read as follows *(changes are indicated)*:

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

3.5.4 Amend table 3.5.2 as follows *(changes are indicated):*

	Category 1 (Category 1A, 1B)	~~**Category 1B**~~	**Category 2**
Symbol	Health hazard	~~Health hazard~~	Health hazard
Signal word	Danger	~~Danger~~	Warning
Hazard statement	May cause genetic defects (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)	~~May cause genetic defects (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)~~	Suspected of causing genetic defects (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)

Chapter 3.6: Carcinogenicity

(see INF.24 (19th session), Annex 1, Item 5)

3.6.3.3 Amend table 3.6.1 as follows *(changes are indicated):*

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

3.6.4 Amend table 3.6.2 as follows *(changes are indicated):*

	Category 1 (Category 1A, 1B)	~~**Category 1B**~~	**Category 2**
Symbol	Health hazard	~~Health hazard~~	Health hazard
Signal word	Danger	~~Danger~~	Warning
Hazard statement	May cause cancer (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)	~~May cause cancer (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)~~	Suspected of causing cancer (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)

Chapter 3.7: Reproductive toxicity

(see INF.24 (19th session), Annex 1, Item 5)

3.7.3.3.2 Amend Table 3.7.1 as follows *(changes are indicated):*

Ingredient classified as:	**Cut-off/concentration limits triggering classification of a mixture as:**			
	Category 1 reproductive toxicant		**Category 2 reproductive toxicant**	**Additional category for effects on or via lactation**
	Category 1A	**Category 1B**		
Category 1A reproductive toxicant	≥ 0.1% (note 1) ≥ 0.3% (note 2)	--	--	--
Category 1B reproductive toxicant	--	≥ 0.1% (note 1) ≥ 0.3% (note 2)	--	--
Category 2 reproductive toxicant	--	--	≥ 0.1% (note 3) ≥ 3.0% (note 4)	--
Additional category for effects on or via lactation	--	--	--	≥ 0.1% (note 1) ≥ 0.3% (note 2)

3.7.4 Amend Table 3.7.1 as follows *(changes are indicated):*

	Category 1 (Category 1A, 1B)	~~**Category 1B**~~	**Category 2**	**Additional category for effects on or via lactation**
Symbol	Health hazard	~~Health hazard~~	Health hazard	*No symbol*
Signal word	Danger	~~Danger~~	Warning	*No signal word*
Hazard statement	May damage fertility or the unborn child (state specific effect if known)(state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)	~~May damage fertility or the unborn child (state specific effect if known) (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)~~	Suspected of damaging fertility or the unborn child (state specific effect if known) (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)	May cause harm to breast-fed children

Chapter 4.1: Hazardous to the aquatic environment

(see INF.24 (19th session), Annex 1 Item 4)

4.1.3.6 Add the following sentence at the end of the existing paragraph:

"The competent authority can decide to specify that the additional statement is communicated on the label or on the SDS or both, or to leave the choice of where to place the statement to the manufacturer/supplier."

4.1.5.1.1 In footnote 3 to the decision logic insert a new second sentence to read as follows:

"The competent authority can decide to specify that the additional statement be communicated on the label or on the SDS or both, or to leave the choice of where to place the statement to the manufacturer/supplier."

4.1.5.2.4 In footnote 10 to the decision logic, insert the following sentence at the end of the existing text:

"The competent authority can decide to specify that the additional statement be communicated on the label or on the SDS or both, or to leave the choice of where to place the statement to the manufacturer/supplier."

Annex 2

[English only]

Bridging principles examples

These examples will be proposed for inclusion in the training document which is being developed by the United Nations Institute for Training and Research (UNITAR) (see UN/SCEGHS/19/INF.24, Annex 2).

1. Dilution bridging principle example

The purpose of this example is to illustrate how the dilution bridging principle criteria can be applied. While this specific example uses acute toxicity data, the reader is reminded that the dilution bridging principle can be applied to other hazard classes as prescribed in the purple book.

Dilution

If a tested mixture is diluted with a diluent that has an equivalent or lower toxicity classification than the least toxic original ingredient, and which is not expected to affect the toxicity of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture. Alternatively, the formula explained in 3.1.3.6.1 could be applied.

Tested mixture information:

Acute toxicity classification and test data		
Oral	**Dermal**	**Inhalation vapours**
Category 4 (LD_{50}: 310 mg/kg)	**Category 4** (LD_{50}: 1250 mg/kg)	**Category 2** (LC_{50}: 1.97 mg/l)

Information on ingredients in the tested mixture:

Ingredient	**Wt%**	**Acute toxicity Classification and Test Data**		
		Oral	**Dermal**	**Inhalation vapours**
Ingredient 1	26	**Category 5** (LD_{50}: 2737 mg/kg)	**Category 4** (LD_{50}: 1500 mg/kg)	**Category 4** (LC_{50}: 11 mg/l)
Ingredient 2	40	**Category 3** (LD_{50}: 118 mg/kg)	**Category 4** (LD_{50}: 1250 mg/kg)	**Category 3** (LC_{50}: 4 mg/l)
Ingredient 3	34	**Category 4** (LD_{50}: 1950 mg/kg)	**Category 4** (LD_{50}: 1100 mg/kg)	**Category 2** (LC_{50}: 1.5 mg/l)

Information on diluent:

Ingredient	Acute toxicity test data		
	Oral	**Dermal**	**Inhalation vapours**
Diluent	**Category 5** (LD_{50}: 2500 mg/kg)	**Category 3** (LD_{50}: 950 mg/kg)	**Category 5** (LC_{50}: 19 mg/l)

Information on an untested mixture:

The tested mixture is diluted 50% with an ingredient that is not expected to affect the toxicity of the other ingredients resulting in the following untested mixture:

Ingredient	Wt%
Ingredient 1	13
Ingredient 2	20
Ingredient 3	17
Diluent	50

Answer:

(a) Oral route – Classification: acute oral toxicity; Category 4

(b) Dermal route – The dilution bridging principle cannot be applied.

(c) Inhalation route – Classification: Acute inhalation toxicity; Category 2

Rationale:

(a) Since acute toxicity test data was not provided for the untested mixture classification via application of substance criteria is not possible;

(b) Classification via the application of bridging principles can be considered since there are sufficient data on both the individual ingredients and a similar tested mixture;

(c) Classification of the mixture based on ingredient information should be considered if the classifier chooses not to apply the bridging principle or sufficient data had not been available to apply the bridging principle;

Oral route

(d) The dilution bridging principle can be applied because the diluent's classification (i.e., Category 5) is an equivalent toxicity classification category as the least toxic original ingredients (i.e., ingredient 1 which is also classified in Category 5);

Dermal route

(e) The dilution bridging principle can not be applied because the diluent's classification (i.e., Category 3) is in a higher toxicity classification category than the least toxic original ingredients (i.e., ingredients 1, 2, and 3 are all classified in Category 4);

(f) Classification of the mixture based on ingredient data should be considered;

Inhalation route

(g) The dilution bridging principle can be applied because the diluent's classification (i.e., Category 5) is in a lower toxicity classification category as the least toxic original ingredients (i.e., ingredient 1 is classified in Category 4).

(End of example 1)

2. Batching bridging principle example

The purpose of this example is to illustrate how the batching bridging principle criteria can be applied. While this specific example uses specific target organ toxicity – single dose data, the reader is reminded that the batching bridging principle can be applied to other hazard classes as prescribed in the purple book.

Batching

The toxicity of a tested production batch of a mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the toxicity of the untested batch has changed. If the latter occurs, a new classification is necessary.

Background

1. Ingredient A is a complex substance that in commercial batches contains a mixture of isomers. Specific target organ toxicity – single exposure effects have been well documented for the ortho-isomers contained in ingredient A.

2. Accidental ingestion of mixtures containing ingredient A in humans due to contamination of drink and food has been reported which resulted in paralysis of the lower extremities.

3. Mixtures containing various concentrations of ingredient A have been tested over the course of many years in animal studies. The results of these studies show a direct correlation of Ingredient A's ortho-isomers concentration in the mixture to statistically significant effects in the animal studies. Based on all available data a conservative guideline is established (i.e., using a safety factor of 1000x) that any mixture containing greater than or equal to 0.5% of the ortho-isomers of ingredient A must be classified as Specific target organ toxicity – single exposure; Category 2. Mixtures containing less than 0.5% of the ortho-isomers of ingredient A are not classified.

Untested mixture information:

Manufacturing batch	Wt% of ortho-isomer of ingredient A
Batch 1	0.42
Batch 2	0.52

Answer:

(a) Batch 1: Applying the batching bridging principle the Untested Batch 1 mixture does not require classification.

(b) Batch 2: Applying the batching bridging principle the Untested Batch 2 mixture is classified as Specific target organ toxicity – single exposure; Category 2.

Rationale:

(a) Classification via application of substance criteria is not possible since Specific target organ toxicity – single exposure test data was not provided for each batch of the mixture;

(b) Classification via the application of bridging principles can be considered since there are sufficient data on both the individual ingredients and similar tested mixtures;

(c) The batching bridging principle can be applied because the tested product batches of the mixture can be assumed to be substantially equivalent to the untested production batches of the same commercial product. In those cases where there is a reason to believe that a significant variation impacts the toxicity of the batch (i.e. based on the ortho-isomer concentration) then a new classification is necessary (e.g. batch 2).

(End of example 2)

3. Concentration of highly toxic mixtures bridging principle example

The purpose of this example is to illustrate how the concentration of highly toxic mixtures bridging principle criteria can be applied. While this specific example uses acute toxicity data, the reader is reminded that the concentration of highly toxic mixtures bridging principle can be applied to other hazard classes as prescribed in the purple book.

Concentration of highly toxic mixtures

If a tested mixture is classified in Category 1, and the concentration of the ingredients of the tested mixture that are in Category 1 is increased, the resulting untested mixture should be classified in Category 1 without additional testing.

Tested mixture information:

Acute toxicity classification and test data	
Oral	**Dermal**
Category 1 (LD_{50}: 3 mg/kg)	**Category 2** (LD_{50}: 85 mg/kg)

Information on ingredients in the tested mixture:

Ingredient	**Wt%**	**Acute toxicity Classification and Test Data**	
		Oral	**Dermal**
Ingredient 1	75	**Category 1** (LD_{50}: 1 mg/kg)	**Category 2** (LD_{50}: 195 mg/kg)
Ingredient 2	25	**Category 2** (LD_{50}: 6 mg/kg)	**Category 1** (LD_{50}: 40 mg/kg)

Information on an untested mixture:

Ingredient	Wt%
Ingredient 1	80
Ingredient 2	20

Answer:

(a) Oral route – Applying the concentration of highly toxic mixtures bridging principle, the untested mixture can be classified as Oral Acute Toxicity; Category 1 without additional testing

(b) Dermal route – Concentration of highly toxic mixtures bridging principle cannot be applied.

Rationale:

(a) Classification via application of substance criteria is not possible since acute toxicity test data was not provided for the untested mixture;

(b) Classification via the application of bridging principles can be considered since there are sufficient data on both the individual ingredients and a similar tested mixture;

(c) Classification of the mixture based on ingredient information should be considered if the classifier chooses not to apply the bridging principle or sufficient data had not been available to apply the bridging principle;

Oral route

(d) The concentration of highly toxic mixtures bridging principle can be applied because the tested mixture is classified in Category 1 and the concentration of ingredient 1 (i.e., a Category 1 ingredient) has increased in the untested mixture.

Dermal route

(e) The concentration of highly toxic mixtures bridging principle cannot be applied because the tested mixture is not classified into Category 1.

(End of example 3)

4. Interpolation within one toxicity category bridging principle example

The purpose of this example is to illustrate how the interpolation within one toxicity category bridging principle criteria can be applied. While this specific example uses skin corrosion/irritation data, the reader is reminded that the interpolation within one toxicity category bridging principle can be applied to other hazard classes as prescribed in the purple book.

Interpolation within one toxicity category

For three mixtures (A, B and C) with identical ingredients, where mixtures A and B have been tested and are in the same irritation/corrosion toxicity category, and where untested mixture C has the same toxicologically active ingredients as mixtures A and B but has concentrations of toxicologically active ingredients intermediate to the concentrations in mixtures A and B, then mixture C is assumed to be in the same irritation/corrosion category as A and B.

Tested mixture information:

Skin corrosion/irritation classification and test data	
Mixture A	**Mixture B**
Skin Irritation; Category 2	**Skin Irritation; Category 2**
Animal 1: Mean Erythema/eschar: 2.5 Mean Oedema: 1.5	Animal 1: Mean Erythema/eschar: 3.8 Mean Oedema: 2.5
Animal 2: Mean Erythema/eschar: 2.3 Mean Oedema: 1.3	Animal 2: Mean Erythema/eschar: 3.5 Mean Oedema: 2.9
Animal 3: Mean Erythema/eschar: 2.2 Mean Oedema: 1	Animal 3: Mean Erythema/eschar: 4.0 Mean Oedema: 3.2

Information on ingredients in the tested mixture:

Ingredient	**Ingredient classification**	**Weight %**	
		Mixture A	**Mixture B**
Ingredient 1	Skin Corrosive; Category 1C	1	5
Ingredient 2	Skin Irritant Category 2	15	30
Water	Not Classified	84	65

Untested mixture information:

Ingredient	**Weight %**		
	Mixture A	**Mixture C**	**Mixture B**
Ingredient 1	1	4	5
Ingredient 2	15	20	30
Water	84	76	65

Answer:

Applying the interpolation within one toxicity category bridging principle the untested Mixture C can be classified as Skin Irritant; Category 2 without additional testing.

Rationale:

(a) Classification via application of substance criteria is not possible since skin corrosion/irritation test data was not provided for the untested mixture;

(b) Classification via the application of bridging principles can be considered since there are sufficient data on both the individual ingredients and a similar tested mixture;

(c) Classification of the mixture based on ingredient information should be considered if the classifier chooses not to apply the bridging principle or sufficient data had not been available to apply the bridging principle;

(d) The interpolation within one toxicity category bridging principle can be applied because:

(i) Mixtures A and B have both been tested and are in the same irritation/corrosion toxicity category (i.e., Skin Irritant; Category 2); AND

(ii) Untested Mixture C has the same toxicologically active ingredients (i.e., ingredients 1 and 2) as tested Mixtures A and B; AND

(iii) The concentrations of ingredients 1 and 2 in Mixture C are both intermediate to the concentrations of ingredients 1 and 2 in Mixtures A and B.

(End of example 4)

5. Substantially similar mixtures bridging principle example

The purpose of this example is to illustrate how the substantially similar mixtures bridging principle criteria can be applied. While this specific example uses skin sensitization data, the reader is reminded that the substantially similar mixtures bridging principle can be applied to other hazard classes as prescribed in the purple book.

Substantially similar mixtures

Given the following:

(a) Two mixtures: (i) A + B;

(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Ingredient B is a sensitizer and ingredients A and C are not sensitizers;

(e) A and C are not expected to affect the sensitizing properties of B.

If mixture (i) or (ii) is already classified based on test data, then the other mixture can be assigned the same hazard category.

Background information:

1. Ingredient 1 has been used in products ranging from 1.2 to 6.0 weight percent for years without reports of sensitization.

2. Existing animal test data on ingredient 1 indicates that it is a Category 1 skin sensitizer.

3. Ingredients 2(a) and 2(b) are analogous lubricant materials with slightly different viscosities. Ingredients 2(a) and 2(b) have both been tested in animal studies and are not skin sensitizers. They are not expected to affect the sensitization potential of ingredient 1.

4. There are no data to suggest that the other ingredients are skin sensitizers or that they will affect the sensitization potential of ingredient 1.

5. Products containing ingredient 1 were then tested in animal studies, which were all negative. Subsequently, clinical study data were gathered and are summarized below:

Tested mixture information:

Product name	Wt% of ingredient 1 in product	Repeated insult patch tests # of positive cases/# Tested
Product 1	5.0	0/298
Product 2	6.0	0/198
Product 3	6.0	0/307
Product 4	5.0	0/197
Product 5	2.5	0/103
		Total: 0/1103

Detailed composition of tested mixture and substantially similar untested mixture:

Tested Mixture (Product 1)	
Ingredient	**Wt%**
Ingredient 1	5.0
Ingredient 2(a)	91.0
Ingredient 3	3.0
Ingredient 4	0.9
Ingredient 5	0.1

Untested Mixture (Product 6)	
Ingredient	**Wt%**
Ingredient 1	4.8
Ingredient 2(b)	91.2
Ingredient 3	3.0
Ingredient 4	0.9
Ingredient 5	0.1

Answer:

The untested mixture (Product 6) is not classified based on the test data available for the similar tested mixture (Product 1).

Rationale:

(a) Classification via application of substance criteria is not possible since skin sensitization test data was not provided for the untested mixture;

(b) Classification via the application of bridging principles can be considered since there are sufficient data on both the individual ingredients and a similar tested mixture;

(c) Classification of the mixture based on ingredient information should be considered if the classifier chooses not to apply the bridging principle or sufficient data had not been available to apply the bridging principle;

(d) As illustrated using the figure below, the substantially similar mixtures bridging principle can be applied because:

(i) The concentration of ingredient B (i.e., ingredient 1 in both mixtures) is essentially the same in both mixtures

(ii) Ingredient B is a sensitizer and ingredients A (i.e., ingredients 2(a), 3, 4, 5) in mixture (i) and C (i.e., ingredients 2(b), 3, 4, 5) in mixture (ii) are not sensitizers

(iii) Ingredients A and C are not expected to affect the sensitizing properties of ingredient B.

(iv) Since product 1 was already not classified based on test data, then product 6 is also not classified based on the test data.

(End of example 5)

6. Aerosols bridging principle example

The purpose of this example is to illustrate how the aerosols bridging principle criteria can be applied. While this specific example uses skin corrosion/irritation data, the reader is reminded that the aerosols bridging principle can be applied to other hazard classes as prescribed in the purple book.

Aerosols

An aerosol form of the mixture may be classified in the same hazard category as the tested non-aerosolized form of the mixture provided that the added propellant does not affect the irritation or corrosive properties of the mixture upon spraying.

Tested mixture information:

Skin Corrosion/Irritation test data
Animal 1: Mean Erythema/eschar: 3.8 Mean Oedema: 2.5
Animal 2: Mean Erythema/eschar: 3.5 Mean Oedema: 2.9
Animal 3: Mean Erythema/eschar: 4.0 Mean Oedema: 3.2

Based on the test data the mixture is classified: Skin Irritant; Category 2

The tested mixture is aerosolized using a 50/50 mixture of propane/butane as the propellant.

Aerosolized untested mixture information:

Ingredient	Weight %
Tested mixture	50
Liquefied propane	25
Liquefied butane	25

Answer:

Applying the aerosols bridging principle the aerosolized untested mixture can be classified as Skin Irritant; Category 2 without additional testing.

Rationale:

(a) Classification via application of substance criteria is not possible since skin corrosion/irritation test data was not provided for the aerosolized untested mixture;

(b) Classification via the application of bridging principles can be considered since there are sufficient data on both the individual ingredients and a similar tested mixture;

(c) The aerosols bridging principle can be applied because:

(i) The non-aerosolized mixture has been tested, and

(ii) The propellant (i.e. 50/50 mixture of liquefied propane/butane) is not corrosive or an irritant, and

(iii) The propellant will not affect the irritation properties of the mixture upon spraying.

(End of example 6)

Annex 3

[English only]

Hazardous to the aquatic environment examples

These examples will be proposed for inclusion in the training document which is being developed by the United Nations Institute for Training and Research (UNITAR) (see UN/SCEGHS/19/INF.24, Annex 3):

Example 1

The following example demonstrates application of the acute additivity methods when only acute toxicity data are available for all of the components of a mixture and then applying the summation method. Ingredients 1, 2, and 3 in this mixture are not classified into chronic categories because Ingredients 1, 2, and 3 are ready biodegradable and have experimentally determined bioconcentration factors (BCF) < 500.

Ingredient information:

Ingredient	Wt%	Acute toxicity data	$L(E)C_{50}$	Classification
Ingredient 1	20	Fish (96 hr LC_{50})	0.15	Acute 1 M-Factor = 1
		Crustacea (48 hr EC_{50})	11	
		Algae /aquatic plants (72 or 96 hr ErC_{50})	33	
Ingredient 2	20	Fish (96 hr LC_{50})	12	Acute 2
		Crustacea (48 hr EC_{50})	1.2	
		Algae /aquatic plants (72 or 96 hr ErC_{50})	43	
Ingredient 3	60	Fish (96 hr LC_{50})	98	Acute 3
		Crustacea (48 hr EC_{50})	91	
		Algae /aquatic plants (72 or 96 hr ErC_{50})	95	

Answer:

Mixture is Acute Category 1, M-Factor 1

Additivity formula

Applying the acute additivity formula from 4.1.3.5.2 (a):

$$\frac{\sum Ci}{L(E)C_{50_m}} = \sum_n \frac{Ci}{L(E)C_{50_i}}$$

Where:

C_i	=	concentration of ingredient i (weight percentage);
$L(E)C_{50}$	=	LC_{50} or EC_{50} for ingredient i, in (mg/l);
N	=	number of ingredients, and i is running from 1 to n;
$L(E)C_{50_m}$	=	$L(E)C_{50}$ of the part of the mixture with test data;

Fish $LC_{50Mixture}$ = 100/(20/0.15 + 20/12 + 60/98) = 0.74 mg/l

Crustacea $EC5_{0Mixtur}$e = 100/(20/11 + 20/1.2 + 60/91) = 5.22 mg/l

Algae $ErC_{50Mixture}$ = 100/(20/33 + 20/43 = 60/95) = 58.73 mg/l

Classification from additivity method: Category 1, M-Factor 1

Summation method

Acute 1: (Acute 1) x M ≥ 25%

using data from ingredients of the mixture:

(20% x 1) = 20% (Not classified)

Acute 2: (M x 10 x Acute 1) + Acute 2 ≥ 25%

using data from ingredients of the mixture:

(1 x 10 x 20%) + 20% = 220% (Classified)

Classification from summation method: Acute Category 2

Rationale:

(a) Classification via application of substance criteria is not possible since acute aquatic toxicity test data was not provided for the mixture as a whole (paragraph 4.1.3.3);

(b) Classification via the application of bridging principles is not possible since data on a similar mixture was not provided (paragraph 4.1.3.4);

(c) Classification based on ingredient data for the mixture can be considered (paragraph 4.1.3.5);

(d) Adequate toxicity data is available for more than one ingredient so the additivity formulas can be considered (paragraph 4.1.3.5.2);

(e) Classification of the mixture based on the acute summation method should be considered (paragraph 4.1.3.5.5) if the additivity formula is not applied;

(f) Applying the “relevant ingredients” concept from paragraph 4.1.3.1 means that ingredients 1, 2, and 3 will be considered when applying the acute additivity formula (paragraph 4.1.3.5.2 (a)) and the summation method (paragraph 4.1.3.5.5).

(g) Since the mixture was classified in more than one way, the method yielding the more conservative result was used (paragraph 4.1.3.5.4);

Additivity formula

(g) All ingredients have acute aquatic toxicity data available for all taxonomic groups (i.e. fish, crustacean and algae) so the toxicity was calculated for each taxonomic group and the lowest value (i.e. Fish) was used to determine the classification (paragraph 4.1.3.5.3);

Summation method

(h) The summation method for acute categories described in paragraph 4.1.3.5.5.3 applies and the cut-off value/concentration limits provided in Table 4.1.3 are used for classification.

(End of example 1)

Example 2

The following example demonstrates application of the acute and chronic summation methods when classification information is available for some or all of the ingredients of a mixture but the $L(E)C_{50}$ data upon which classification is based are not available to the classifier of the mixture.

Ingredient information:

Ingredient	Wt%	Acute classification (M-factor)	Chronic classification (M-factor)
Ingredient 1	0.01	Acute 1 (M-factor: 10)	Chronic 1 (M-factor: 10)
Ingredient 2	1.0	Acute 2	Chronic 2
Ingredient 3	25.0	Not classified	Chronic 4
Ingredient 4	68.76	Not classified	Not classified

Answer:

Acute Classification - Not classified because:

Acute 1: (Acute 1) x M ≥ 25%

using data from ingredients of the mixture:

(0.01% x 10) = 0.1% (Not classified)

Acute 2: (M x 10 x Acute 1) + Acute 2 ≥ 25%

using data from ingredients of the mixture:

(10 x 10 x 0.01%) + 1.0% = 2.0% (Not classified)

Acute 3: (M x 100 x Acute 1) + (10 x Acute 2) + Acute 3 ≥ 25%

using data from ingredients of the mixture:

(10 x 100 x 0.01%) + (10 x 1.0) = 20% (Not classified)

Chronic Classification - Category 4 because:

Chronic 1: (Chronic 1) x M ≥ 25%

using data from ingredients of the mixture:

0.01% x 10 = 0.1% (Not classified)

Chronic 2: (M x 10 x Chronic 1) + Chronic 2 ≥ 25%

using data from ingredients of the mixture:

(10 x 10 x 0.01%) + 1.0% = 2% (Not classified)

Chronic 3: (M x 100 x Chronic 1) + (10 x Chronic 2) + Chronic 3 ≥ 25%

using data from ingredients of the mixture:

(10 x 100 x 0.01%) + (10 x 1.0%) = 20% (Not classified)

Chronic 4: Chronic 1 + Chronic 2 + Chronic 3 + Chronic 4 ≥ 25%

using data from ingredients of the mixture:

0.01% + 1.0% + 25.0% = 26.01% (Classified)

Rationale:

(a) Classification via application of substance criteria is not possible since aquatic toxicity test data was not provided for the mixture (paragraph 4.1.3.3);

(b) Classification via the application of bridging principles is not possible since data on a similar mixture was not provided (paragraph 4.1.3.4);

(c) Classification based on ingredient data for the mixture can be considered (paragraph 4.1.3.5);

(d) Adequate toxicity data is not available so the additivity formulas cannot be considered (paragraph 4.1.3.5.2);

(e) Acute and chronic classification data is available for some of the ingredients of the mixture so the summation method can be considered (paragraph 4.1.3.5.5);

Acute classification:

(f) Applying the "relevant ingredients" concept from paragraph 4.1.3.1 means that:

(i) The use of expert judgment is necessary to make the "relevant ingredient" decision for ingredient 1 since it is a highly toxic ingredient with an M-factor of 10. In this case it was decided to include the ingredient because its concentration in the mixture (i.e., 0.01%) is still significant given the M factor and the constants used in the Acute 2 and 3 calculations for Acute 1 ingredients;

(ii) Ingredient 2 will be included in the calculation because it is in the mixture at a concentration ≥ 1%;

(g) The acute summation method approach described in paragraph 4.1.3.5.5.3 applies and the cut-off value/concentration limits provided in Table 4.1.3 are used for classification.

Chronic classification:

(h) Applying the "relevant ingredients" concept from paragraph 4.1.3.1 means that:

(i) The use of expert judgment is necessary to make the "relevant ingredient" decision for ingredient 1 since it is a highly toxic ingredient with an M-factor of 10. In this case it was decided to include the ingredient because its concentration in the mixture (i.e., 0.01%) is still significant given the M factor and the constants used in the Chronic 2 and 3 calculations for Chronic 1 ingredients.

(ii) Ingredients 2 and 3 will be included in the calculation because they are in the mixture at a concentration ≥ 1%.

(i) The chronic summation method approach described in paragraph 4.1.3.5.5.4 applies and the cut-off value/concentration limits provided in Table 4.1.4 are used for classification.

(End of example 2)

Example 3

The following example demonstrates application of a stepped approach where the additivity formula is used for the part of the mixture that has chronic toxicity data and passing that result into the chronic summation method.

Ingredient information:

Ingredient	Wt%	Chronic toxicity data	NOEC or EC_x	Rapidly degradable	Classification
Ingredient 1	15	NOEC (28 day for fish)	4.1	Yes	Chronic 3
		NOEC (21 day for crustacea)	0.13		
Ingredient 2	5	NOEC (for algae)	0.8	No	Chronic 2
Ingredient 3	80	Data not provided by supplier			Chronic 3

Answer:

Mixture is Chronic Category 3

Step 1:

Applying the chronic additivity formula from 4.1.3.5.2 (b):

$$\frac{\sum \mathrm{Ci} + \sum \mathrm{Cj}}{\mathrm{EqNOEC}_m} = \sum_n \frac{\mathrm{Ci}}{\mathrm{NOECi}} + \sum_n \frac{\mathrm{Cj}}{0.1 \times \mathrm{NOECj}}$$

where:

C_i = concentration of ingredient i (weight percentage) covering the rapidly degradable ingredients;

Cj = concentration of ingredient j (weight percentage) covering the non- rapidly degradable ingredients;

$NOEC_i$ = NOEC (or other recognized measures for chronic toxicity) for ingredient i covering the rapidly degradable ingredients, in mg/l;

NOECj = NOEC (or other recognized measures for chronic toxicity) for ingredient j covering the non-rapidly degradable ingredients, in mg/l;

N = number of ingredients, and i and j are running from 1 to n;

$EqNOEC_m$ = Equivalent NOEC of the part of the mixture with test data;

EqNOECm = 20/(15/0.13) + 5/(0.1x 0.8) = 0.11 mg/l

The part of the mixture (i.e., 20%) with Chronic toxicity data (i.e., ingredients 1 and 2) has an EqNOECm of 0.11 mg/l. As the NOEC of the ingredients that are considered not-rapidly degradable have already been multiplied with the factor 0.1 the EqNOECm can now be applied to table 4.1 b (ii) resulting in a classification of Chronic 3.

Step 2:

Ingredient information going into the chronic summation method calculations:

Ingredient	Wt %	Classification
Additivity result – part of mixture with toxicity data	20	Chronic 3
Ingredient 3	80	Chronic 3

Chronic 1: (Chronic 1) x M ≥ 25%

0% (Not classified)

Chronic 2: (M x 10 x Chronic 1) + Chronic 2 ≥ 25%

using data from the additivity result & ingredients of the mixture:

(10 x 0%) + 0% = 0% (Not classified)

Chronic 3: (M x 100 x Chronic 1) + (10 x Chronic 2) + Chronic 3 ≥ 25%

using data from the additivity result & ingredients of the mixture:

(100 x 0%) + (10 x 0%) + 20% + 80% = 100% (Classified)

Rationale:

(a) Classification via application of substance criteria is not possible since acute aquatic toxicity test data was not provided for the mixture (paragraph 4.1.3.3);

(b) Classification via the application of bridging principles is not possible since data on a similar mixture was not provided (paragraph 4.1.3.4);

(c) Classification based on ingredient data for the mixture can be considered (paragraph 4.1.3.5);

(d) Adequate toxicity data as well as classification results for the ingredients are available so the additivity formula in combination with the summation method can be considered (paragraphs 4.1.3.5.2 & 4.1.3.5.5.4);

(e) Applying the "relevant ingredients" concept from paragraph 4.1.3.1 means that ingredients 1, 2, and 3 will be considered in the calculations (paragraph 4.1.3.5.2 (b));

(f) When applying the additivity formula the preferred method is to calculate the toxicity of this part of the mixture for each ingredient toxicity values that relate to the same taxonomic group (i.e. fish, crustacean or algae) and then to use the highest toxicity obtained (i.e., use the most sensitive of the three groups). However, when toxicity data for each ingredient are not available in the same taxonomic group the data from the most sensitive test organism should be used (paragraph 4.1.3.5.3). In this case ingredient 1's toxicity data for Crustacea is used because it is has the lowest value (i.e. highest toxicity) and ingredient 2's Algae data is used;

(h) Application of the chronic additivity formula results in 20% of the mixture being classified at Chronic Category 3, which is used in the chronic summation method with the classification information provided for ingredient 3;

(End of example 3)

Example 4

The following example demonstrates application of the tiered approach to determining the mixture's classification where acute toxicity data is available on the mixture as well as on the ingredients, and chronic classification information is only available on the ingredients.

Ingredient information:

Ingredient	Wt%	Acute toxicity data	$L(E)C_{50}$ mg/l	Chronic classification
Ingredient 1	5	LC_{50} (for fish)	12	Chronic 1 (M Factor: 1)
		EC_{50} (for crustacea)	18	
		ErC_{50} (algae)	0.9	
Ingredient 2	1.5	LC_{50} (for fish)	40	Chronic 2
		EC_{50} (for crustacea)	25	
		ErC_{50} (algae)	9.5	
Ingredient 3	93.5	LC_{50} (for fish)	> 100	Chronic 4
		EC_{50} (for crustacea)	> 100	
		ErC_{50} (algae)	> 100	

Information on tested mixture:

Acute toxicity data	$L(E)C_{50}$ mg/l
LC_{50} (for fish)	68
EC_{50} (for crustacea)	90
ErC_{50} (algae)	12.5

Answer:

Acute classification - Category 3

Chronic classification - Category 2 because:

Chronic 1: (Chronic 1) x M ≥ 25%

5% x 1 = 5% (Not classified)

Chronic 2: (M x 10 x Chronic 1) + Chronic 2 ≥ 25%

using data from the ingredients of the mixture:

(1 x 10 x 5%) + 1.5% = 51.5% (Classified)

Rationale:

Acute classification:

(a) Classification via application of substance criteria is possible for acute toxicity since acute aquatic toxicity test data was provided for the mixture (paragraph 4.1.3.3);

(b) The higher toxicity value (from the most sensitive test organism) which in this case is Algae or other aquatic plants is used to classify the tested mixture (paragraph 4.1.3.3.3 (a));

Chronic classification:

(c) Classification via application of substance criteria is not possible since chronic aquatic toxicity test data was not provided for the mixture (paragraph 4.1.3.3.4 (a));

(d) Classification via the application of bridging principles is not possible since data on a similar mixture was not provided (paragraph 4.1.3.4);

(e) Adequate chronic toxicity data is not available so the chronic additivity formulas cannot be considered (paragraph 4.1.3.5.2 (b));

(f) Chronic classification data is available for some of the ingredients of the mixture so the summation method can be considered (paragraph 4.1.3.5.5);

(g) Applying the "relevant ingredients" concept from paragraph 4.1.3.1 means that ingredients 1, 2, and 3 will be considered when applying criteria in paragraph 4.1.3.5.5;

(h) The chronic summation method approach described in paragraph 4.1.3.5.5.4 applies and the cut-off value/concentration limits provided in Table 4.1.4 are used for classification.

(End of example 4)