UN/SCETDG/46/INF.15
UN/SCEGHS/28/INF.7

Committee of Experts on the Transport of Dangerous Goods and on the Globally Harmonized System of Classification and Labelling of Chemicals

4 November 2014

Sub-Committee of Experts on the Transport of Dangerous Goods

Forty-sixth session
Geneva,1–9 December 2014
Item 8 (g) of the provisional agenda
Issues relating to the Globally Harmonized System of Classification and Labelling of Chemicals: corrosivity criteria

Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals

Twenty-eighth session
Geneva, 10–12 (a.m) December 2014
Item 2 (d) of the provisional agenda
Classification criteria and related hazard communication: work of the TDG-GHS working group on corrosivity criteria

Proposal for revision of Chapter 2.8 of the Model Regulations (Amendments to the proposal in ST/SG/AC.10/C.3/2014/69 – ST/SG/AC.10/C.4/2014/12)

Transmitted by the European Chemical Industry Council (CEFIC)

Introduction

1. Reference is made to document ST/SG/AC.10/C.3/2014/69 - ST/SG/AC.10/C.4/2014/12, and presenting the result of the discussion in the intersessional joint TDG-GHS working group on the development of a proposal for a revision of chapter 2.8 by considering the following basic aspects:

- No change in the level of safety for transport.
- The transport conditions will not become more severe.
- No direct change in classification and assignment of the packing group for substances listed by name in the Dangerous Goods List of chapter 3.2.
- Classification criteria for skin corrosivity are consistent between GHS and TDG
- The proposal should not promote the use of tests conducted on animals.

2. CEFIC participated in the working group and generally appreciates the proposal drafted by the Netherlands as a step forward in harmonizing between the sectors of transport (TDG) and supply and use (GHS). CEFIC supports the structural approach to clearly distinguish between hazard classification and assignment of packing groups. The necessity to reproduce the GHS criteria for skin corrosivity in the proposed new chapter 2.8, in the same way as the GHS criteria for environmentally hazardous substances are integrally reproduced in chapter 2.9, is justified by the following situation:

- Not all countries have implemented GHS yet;
- Not all products, which are transported as dangerous goods, are required to be classified according to GHS. For example (veterinary) medicinal products, cosmetic products, food additives, waste, substances and mixtures for scientific research, which are not placed on the market, as well as articles are

not within the scope of the European CLP-regulation. And in other areas of the world, there exist other exemption (e.g. based on listed substances, use of industrial products, industrial versus consumer, etc.) for the implementation of the GHS.

3. CEFIC, however, does not share support for all aspects of the draft provided by the Netherlands. Amendments proposed by CEFIC are explained in the following paragraphs and included in the revised proposal for a new chapter 2.8 presented at the end of this paper.

4. Reference is also made to document ST/SG/AC.10/C.3/2014/99-ST/SG/AC.10/C.4/2014/18. CEFIC appreciates the proposal, however it is a very limited approach to harmonisation with GHS as the major part of alternative methods is not considered. In addition the proposed provisions regarding the extreme pH-value would force to test each substance and mixture with an extreme-pH-value to avoid worst case assignment to packing group I, as other information like the assigned classification and packing groups of the ingredients are not taken into account.

General comments

5. Hazard classification should be limited to the assessment on the intrinsic property of corrosivity, i.e. the identification of the class 8 without sub-classification. The distinction with regard to different levels of risk in transport should take place in the step of assigning the packing group. Although the approach to implement the sub-classification 8A, 8B and 8C has been helpful within the discussion and the process for understanding in which way the criteria of GHS should be introduced to transport, a sub-classification should not become part of the transport regulations. Consequently all parts dealing with sub-classification have been revised in the proposed new text for chapter 2.8 considering the following arguments:

- Not all countries introduced sub categories 1A, 1B, 1C when implementing GHS (e.g. Russia, South Korea, etc.).
- Countries which have implemented the Sub-Categories 1A, 1B and 1C have also implemented legally binding classification lists which strongly differ from each other (e.g. Europe – New Zealand, see also INF.26/Add.1 (TDG, 43rd session) - INF.9/Add.1 (GHS, 25th session).
- Sub-Classification within class 8 due to different levels of risk and not due to different properties would be something new, which is currently not established in the regime of transport classification. This could lead to confusion.
- Especially for classification based on information of the components (additivity and non-additivity approach) the sub-classification would make the process more complicate. The most important source of information for classification in transport is the Dangerous Goods List in chapter 3.2, which shows the harmonized and binding provisions for substances on the level of UN, stipulating the classes, subsidiary risks and packing groups. This information cannot be translated into the sub-classification 8A, 8B and 8C.

6. The description of the tiered evaluation for skin corrosion of substances has been modified (Figure 2.8.1 of the draft) to take into account the following aspects:

- New boxes have been included to clarify the negative response of validated in vitro tests, in order to avoid discrepancy between text and flow chart.

– Replacement of the term “skin corrosion” by “class 8” to be consistent with the language in other parts of the transport regulations.

7. Considering the interpretation of extreme pH-values in case none of the ingredients of a mixture is classified to class 8, the mixture itself needs not to be classified as class 8. Evidence is provided by the following examples: Citric acid, silicates and dental products. The respective chapter has been amended accordingly and examples to illustrate this will be provided in a separate INF paper (INF.14, TDG 46th session – INF.6, GHS 28th session).

8. In analogy to the description of the tiered evaluation for skin corrosion of substances (Figure. 2.8.1) a tiered approach for mixtures has been added as Figure 2.8.2 of the revised draft to keep also consistency with the proposed text.

9. As a consequence of the proposal to limit classification to the assessment on the intrinsic property of corrosivity, i.e. the identification of the class 8 without sub-classification, the assignment of packing groups based on animal testing or in vitro test data (if applicable) has to remain part of the respective chapter 2.8.3 on this topic.

10. For products where no test data are available the procedure of the assignment the packing group has been completed:

– Substances for which only an extreme pH-value is available are assigned to packing group I

– Substances classified on validated structure activity relationship (SAR) are assigned to the appropriate packing group.

– For mixtures the alternative methods should be used.

11. As a consequence when omitting the implementation of sub-classification, the starting point for the additivity approach turns out to be the evaluation of the packing groups of the components of the mixture. The description in Figure 2.8.3 has been amended accordingly in analogy to the non-additivity approach described in Figure 2.8.4 of the revised proposal.

12. In the discussions of the working group the perception crystallized, that the designing of the additivity approach including the concentration limits is a central regulation screw to fulfil the criteria “not to change the level of safety and not to strengthen the requirements for transport” given at the start of the mandate. Based on the figures already communicated in the INF.26 (TDG, 43rd session) - INF.9 (GHS, 25th session) and on further investigations carried out (see INF.14 (TDG, 46th session) – INF.6 (GHS 28th session) CEFIC proposes an additional general concentration limit of 50% for packing group I, 15% for packing group II and 5% for packing group III (details see table 2.8.4 in the attached proposal for chapter 2.8). These values would guarantee gradual assignment of the packing groups and would keep the existing safety level and also the awareness for really hazardous mixtures assigned to PG I. As the current transport conditions proved to be sufficient to guarantee a safe transport, the general concentration limit especially for PG I should be higher in transport than in GHS. The proposed value is based on the evaluations of the current assignments in Industry and on the substances listed by name, which are assigned to specific concentration limits. These specific concentration limits for substances listed by name in the UN Model Regulations assigned to packing group I range between 37% and 70%. Therefore 50% would be in the low third of this range and therefore we think it is an appropriate approach to solve the issue. An additional general concentration limit of 15% has been proposed for packing group II to adjust it to the similar staggered approach that has been proposed for the non additivity approach in the ST/SG/AC.10/C.3/2014/69 - ST/SG/AC.10/C.4/2014/12.

Proposal

Amend the proposal in ST/SG/AC.10/C.3/2014/69 - ST/SG/AC.10/C.4/2014/12 of chapter 2.8 as submitted by the Netherlands as follows (text underlined is changed):

“Chapter 2.8

Class 8 – Corrosive substances

2.8.1 Definitions and general provisions

2.8.1.1 *Class 8 (corrosive) substances* are substances which, by chemical action, lead to the production of irreversible damage to the skin; namely, visible necrosis through the epidermis and into the dermis, following the application of a test substance for up to 4 hours and observation periods of up to 14 days, or, in the case of leakage, will materially damage, or even destroy, other goods or the means of transport.

2.8.1.2 For substances and mixtures that are corrosive to skin, hazard classification is determined using criteria in section 2.8.2. Substances or mixtures shall be classified in ~~one of the three sub-classifications 8A, 8B or 8C~~ class 8. ~~Where the available data do not allow sub-classification, substances and mixtures shall be assigned to Class 8 without sub-classification~~. Substances and mixtures corrosive to skin are assigned to a packing group using criteria in section 2.8.3.

~~***NOTE:*** *The sub-classifications 8A, 8B and 8C do not constitute divisions in Class 8.*~~

2.8.1.3 Liquids and solids which may become liquid during transport, which are judged not to be skin corrosive shall still be considered for their potential to cause corrosion to certain metal surfaces in accordance with the criteria in 2.8.4.

2.8.1.4 A substance or a mixture meeting the criteria of Class 8 having an inhalation toxicity of dusts and mists (LC_{50}) in the range of packing group I, but toxicity through oral ingestion or dermal contact only in the range of packing group III or less, shall be allocated to Class 8 (see Note under 2.6.2.2.4.1).

2.8.2 Criteria for hazard classification of substances or mixtures as corrosive to skin

For hazard classification of a substance or a mixture into Class 8, all available information on corrosive properties of a substance or a mixture shall be taken into account in a tiered approach (see 2.8.2.2). Emphasis shall be placed upon existing human data, followed by existing animal data, followed by *in vitro* data and then other sources of information. Classification results directly when the data satisfy the criteria. In some cases, classification of a substance or a mixture is made on the basis of the weight of evidence within a tier. In a total weight of evidence approach all available information bearing on the determination of skin corrosion is considered together, including the results of appropriate validated *in vitro* tests, relevant animal data, and human data such as epidemiological and clinical studies and well-documented case reports and observations.

2.8.2.1 *Hazard classification corrosive to skin based on standard animal test data*

2.8.2.1.1 A substance is corrosive to skin when it produces destruction of skin tissue, namely, visible necrosis through the epidermis and into the dermis, in at least one tested animal after exposure for up to 4 hours. An example of an internationally accepted validated test method for skin corrosion is OECD Test Guideline 404[1] .

~~2.8.2.1.2 Three sub-categories are provided within the corrosion Class (Class 8, see Table 2.8.1): Class 8A, where corrosive responses are noted following up to 3 minutes exposure and up to 1 hour observation; Class 8B, where corrosive responses are described following exposure greater than 3 minutes and up to 1 hour and observations up to 14 days; and Class 8C, where corrosive responses occur after exposures greater than 1 hour and up to 4 hours and observations up to 14 days.~~

Table 2.8.1: Skin corrosion hazard classification[a]

	Criteria
Class 8	Destruction of skin tissue, namely, visible necrosis through the epidermis and into the dermis, in at least one tested animal after exposure ≤ 4 h and during an observation time of up to 14 days.
~~**Class 8A**~~	~~Corrosive responses in at least one animal following exposure ≤ 3 min during an observation period ≤ 1 h~~
~~**Class 8B**~~	~~Corrosive responses in at least one animal following exposure > 3 min and ≤ 1 h and observations ≤ 14 days~~
~~**Class 8C**~~	~~Corrosive responses in at least one animal after exposures > 1 h and ≤ 4 h and observations ≤ 14 days~~

[a] *The use of human data is addressed in GHS 3.2.2.2 and in GHS chapters 1.1 (par. 1.1.2.5 (c)) and 1.3 (par.. 1.3.2.4.7).*

2.8.2.2 Hazard classification in a tiered approach

2.8.2.2.1 Hazard classification criteria for substances

2.8.2.2.1.1 A *tiered approach* to the evaluation of initial information shall be considered, where applicable (Figure 2.8.1), recognizing that not all elements may be relevant.

2.8.2.2.1.2 Existing human and animal data including information from single or repeated exposure shall be the first line of evaluation, as they give information directly relevant to effects on the skin.

2.8.2.2.1.3 Acute dermal toxicity data may be used for classification. If a substance is highly toxic by the dermal route, a skin corrosion/irritation study may not be practicable since the amount of test substance to be applied would considerably exceed the toxic dose and, consequently, would result in the death of the animals. When observations are made of skin corrosion in acute toxicity studies and are observed up through the limit dose, these data shall be used for classification provided that the dilutions used and species tested are equivalent. Solid substances (powders) may become corrosive or irritant when moistened or in contact with moist skin or mucous membranes.

[1] *OECD Guideline for the testing of chemicals No. 404 "Acute Dermal Irritation/Corrosion" 2002.*

2.8.2.2.1.4 In vitro alternatives that have been validated and accepted can be used to make classification decisions. Examples of internationally accepted validated test methods for skin corrosion include OECD Test Guidelines 430[1] (Transcutaneous Electrical Resistance Test (TER)), 431[2] (Human Skin Model Test) and 435 (Membrane Barrier Test Method)[3]. Some in vitro tests are suitable to sub-classify. A substance which is determined not to be corrosive in accordance with OECD Test Guideline 430 or 431 may be considered not to be corrosive to skin for the purposes of these Regulations.

2.8.2.2.1.5 Likewise, pH extremes like ≤ 2 and ≥ 11.5 may indicate skin effects, especially when associated with significant acid/alkaline reserve (buffering capacity). Generally, such substances are expected to produce significant effects on the skin. In the absence of any other information, a substance is considered corrosive (Class 8) if it has a $pH \leq 2$ or a $pH \geq 11.5$. However, if consideration of acid/alkaline reserve[4] suggests the substance may not be corrosive despite the low or high pH value, this needs to be confirmed by other data, preferably by data from an appropriate validated in vitro test.

2.8.2.2.1.6 In some cases sufficient information may be available from structurally related substances to make classification decisions.

2.8.2.2.1.7 The tiered approach provides guidance on how to organize existing information on a substance and to make a weight of evidence decision about hazard assessment and hazard classification (ideally without conducting new animal tests). Although information might be gained from the evaluation of single parameters within a tier (see 2.8.2.2.1), consideration shall be given to the totality of existing information and making an overall weight of evidence determination. This is especially true when there is conflict in information available on some parameters.

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1 *OECD Guideline for the testing of chemicals No. 430 "In Vitro Skin Corrosion: Transcutaneous Electrical Resistance Test (TER)" [2004][2013].*

2 *OECD Guideline for the testing of chemicals No. 431 "In Vitro Skin Corrosion: Human Skin Model Test" [2004][2013].*

3 *OECD Guideline for the testing of chemicals No. 435 "Membrane Barrier Test Method" 2006.*

4 *Acid/Alkaline reserve may be determined e.g. by the methodology detailed in Young J.R., How M.J., Walker A.P., Worth W.M.H. (1988): Classification as corrosive or irritant to skin of preparations containing acidic or alkaline substances, without testing on animals. Toxicology in Vitro **2**, 19-26 and Young J.R., How M.J. (1994): Product classification as corrosive or irritant by measuring pH and acid / alkali reserve. In Alternative Methods in Toxicology vol. 10 - In Vitro Skin Toxicology: Irritation, Phototoxicity, Sensitization, eds. A.Rougier, A.M. Goldberg and H.I.Maibach, Mary Ann Liebert, Inc. 23-27.*

Figure 2.8.1: Tiered evaluation for skin corrosion (substances)			
Step	**Parameter**	**Finding**	**Conclusion**
1a:	Existing human or animal skin corrosion data [a] →	Skin corrosive →	Classify as ~~**skin corrosive**~~ **class 8**[b]
	↓ Not corrosive/No data ↓		
1b:	Existing human or animal skin corrosion data [a] →	Not a skin corrosive →	**Not classified as Class 8 (in case it is not corrosive to metals)**
	↓ No/Insufficient data ↓		
2:	Other existing skin data in animals [c] →	Yes; other existing data showing that substance may cause skin corrosion →	May be deemed to be a ~~**skin corrosive**~~ **class 8** [b]
	↓ No/Insufficient data ↓		
3a:	Existing *ex vivo/in vitro* data [d] →	Positive on corrosivity: Skin corrosive →	Classify as ~~**skin corrosive**~~ **class 8**[b]
	↓ ~~No/Insufficient data/~~Negative response ↓		

Figure 2.8.1: Tiered evaluation for skin corrosion (substances)			
Step	**Parameter**	**Finding**	**Conclusion**
3b:	Existing ex vivo/in vitro data [e] → ↓ No/insufficient data ↓	Negative response on corrosivity: Not a skin corrosive →	Not classified as Class 8 (in case it is not corrosive to metals)
4:	pH-Based assessment (with consideration of acid/alkaline reserve of the chemical) [f] → ↓ Not pH extreme, no pH data or extreme pH with data showing low/no acid/alkaline reserve ↓	pH ≤ 2 or ≥ 11.5 with high acid/alkaline reserve or no data for acid/alkaline reserve →	Classify as ~~**skin corrosive**~~ **class 8**
5:	Validated Structure Activity Relationship (SAR) methods → ↓ No/Insufficient data ↓	Skin corrosive →	Deemed to be ~~**skin corrosive**~~ **class 8** [b]
6:	Consideration of the total weight of evidence [g] → ↓	Skin corrosive →	Deemed to be ~~**skin corrosive**~~ **class 8** [b]
7:	~~**Not classified**~~ **Not classified as Class 8 (in case it is not corrosive to metals)**		

[a] *Existing human or animal data could be derived from single or repeated exposure(s), for example in occupational, consumer, transport, or emergency response scenarios; or from purposely-generated data from animal studies conducted according to validated and internationally accepted test methods. Although human data from accident or poison centre databases can provide evidence for classification, absence of incidents is not itself evidence for no classification as exposures are generally unknown or uncertain;*

[b] *Classify in Class 8/~~sub-classification~~, as applicable;*

[c] *All existing animal data shall be carefully reviewed to determine if sufficient skin corrosion evidence is available. In evaluating such data, however, the reviewer shall bear in mind that the*

reporting of dermal lesions may be incomplete, testing and observations may be made on a species other than the rabbit, and species may differ in sensitivity in their responses;

[d] *Evidence from studies using validated protocols with isolated human/animal tissues or other, non-tissue-based, though validated, protocols shall be assessed. Examples of internationally accepted, validated test methods for skin corrosion include OECD Test Guideline 430 (Transcutaneous Electrical Resistance Test (TER)), 431 (Human Skin Model Test), and 435 (Membrane Barrier Test Method).*

[e] *in accordance to 2.8.2.2.4.1.4*

[f] *Measurement of pH alone may be adequate, but assessment of acid or alkali reserve (buffering capacity) would be preferable. Presently, there is no validated and internationally accepted method for assessing this parameter;*

[g] *All information that is available shall be considered and an overall determination made on the total weight of evidence. This is especially true when there is conflict in information available on some parameters. Expert judgment shall be exercised prior to making such a determination. Negative results from applicable validated skin corrosion/irritation in vitro tests are considered in the total weight of evidence evaluation.*

2.8.2.~~3~~.2.2 Hazard classification criteria for mixtures

2.8.2.~~3~~.2.2.1 Hazard classification of mixtures when data are available for the complete mixture

2.8.2.~~3~~.2.2.1.1The mixture shall be classified using the criteria for substances, taking into account the tiered approach to evaluate data for Class 8 (as illustrated in Figure 2.8.1, step 1 - 3).

~~2.8.2.3. 2.1. When considering testing of the mixture, classifiers are encouraged to use a tiered weight of evidence approach as included in the criteria for classification of substances for skin corrosion to help ensure an accurate classification, as well as to avoid unnecessary animal testing. In the absence of any other information, a mixture is considered corrosive (Class 8) if it has a pH ≤ 2 or a pH ≥ 11.5. However, if consideration of acid/alkaline reserve[5] suggests the mixture may not be corrosive despite the low or high pH value, this needs to be confirmed by other data, preferably by data from an appropriate validated in vitro test.~~

Paragraph 2.8.2.3.2.1 moved further down

2.8.2.~~3~~.2.2.2 Hazard classification of mixtures when data are not available for the complete mixture: bridging principles

2.8.2.~~3~~.2.2.2.1Where the mixture itself has not been tested to determine its skin corrosion potential, but there are sufficient data on both the individual ingredients and similar tested mixtures to adequately characterize the hazards of the mixture, these data will be used in accordance with the following agreed bridging principles. This ensures that the classification process uses the available data to the greatest extent possible in characterizing the hazards of the mixture without the necessity for additional testing in animals.

2.8.2.~~3~~.2.2.2.2 Dilution

If a tested mixture is diluted with a diluent which has an equivalent or lower corrosivity classification than the least corrosive original ingredient and which is not expected to affect the corrosivity of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture. Alternatively, the method explained in 2.8.2.3.3 could be applied.

2.8.2.~~3~~.2.2.2.3 Batching

The skin corrosion potential 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 skin corrosion potential of the untested batch has changed. If the latter occurs, a new classification is necessary.

2.8.2.3.2.2.2.4 Concentration of mixtures of the highest corrosion sub-classification

If a tested mixture classified ~~in the highest sub-classification for~~ as skin corrosion is concentrated, the more concentrated untested mixture shall be classified ~~in the highest corrosion sub-classification~~ as class 8 without additional testing.

2.8.2.~~3~~.2.2.2.5 Interpolation within ~~one sub-classification~~ class 8

For three mixtures (X, Y and Z) with identical ingredients, where mixtures X and Y have been tested and are ~~in the same skin corrosion sub-classification~~ class 8, and where untested mixture Z has the same toxicologically active ingredients as mixtures X and Y but has concentrations of toxicologically active ingredients intermediate to the concentrations in mixtures X and Y, then mixture Z is assumed to be ~~in the same skin corrosion sub-classification~~ class 8 as X and Y.

2.8.2.~~3~~.2.2.2.6 Substantially similar mixtures

Given the following:

(a) Two mixtures: (i) X + Y;

(ii) Z + Y;

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

(c) The concentration of ingredient X in mixture (i) equals that of ingredient Z in mixture (ii);

(d) Data on skin corrosion for X and Z are available and substantially equivalent, i.e. they are in the same class ~~sub-classification~~ and are not expected to affect the skin corrosion potential of Y.

If mixture (i) or (ii) is already classified based on test data, then the other mixture can be classified in ~~the same sub-classification~~ class 8.

2.8.2.~~3~~.2.2.3 *Hazard classification of mixtures ~~when~~ where no data for the complete mixture are available but when data are available for all ingredients or only for some ingredients of the mixture*.

2.8.2.~~3~~.2.2.3.1 In order to make use of all available data for purposes of classifying the skin corrosion hazards of mixtures, the following assumption has been made and is applied where appropriate in the tiered approach (see Table 2.8.2):

The "relevant ingredients" of a mixture are those which are present in concentrations ≥ 1% (w/w for solids, liquids, dusts, mists and vapours and v/v for gases), unless there is a presumption that an ingredient present at a concentration < 1% can still be relevant for classifying the mixture for skin corrosion.

2.8.2.~~3~~.2.2.3.2 Additivity

In general, the approach to classification of mixtures as corrosive to skin when data are available on the ingredients, but not on the mixture as a whole, is based on the theory of additivity, such that each skin corrosive ingredient contributes to the overall corrosive properties of the mixture in proportion to its potency and concentration. The mixture is classified as corrosive when the sum of the concentrations of such ingredients exceeds a cut-off value/concentration limit.

2.8.2.~~3~~.2.2.3.3 Where the sum of all ingredients of a mixture ~~sub-classified 8A, 8B or 8C~~ is ~~each~~ ≥ 5% the mixture shall be classified as class 8. ~~skin sub-classification 8A, 8B or 8C, respectively. Where the sum of 8A ingredients is < 5% but the sum of 8A + 8B ingredients is ≥ 5%, the mixture shall be classified as sub-classification 8B. Similarly, where the sum of 8A + 8B ingredients is < 5% but the sum of 8A + 8B + 8C ingredients is ≥ 5% the mixture shall be classified as sub-classification 8C. Where at least one relevant ingredient in a mixture is classified as Class 8 without sub-classification, the mixture shall be classified as Class 8 without sub-classification if the sum of all ingredients corrosive to skin is ≥ 5%.~~

2.8.2.~~3~~.2.2.3.4 Non-additivity

Particular care must be taken when classifying certain types of chemicals such as acids and bases, inorganic salts, aldehydes, phenols, and surfactants. The approach explained in ~~2.8.2.3.3.2 and~~ 2.8.2.~~3~~.2.2.3.3 might not work given that many such substances are corrosive at concentrations < 1%. For mixtures containing strong acids or bases the pH shall be used as classification criterion (see 2.8.2.~~3.1.2.~~2.2.3.5) since pH will be a better indicator of corrosion than the concentration limits in 2.8.2.~~3~~.2.2.3.3. A mixture containing corrosive ingredients that cannot be classified based on the additivity approach due to chemical characteristics that make this approach unworkable, shall be classified as Class 8 if it contains ≥ 1% of a corrosive ingredient. Classification of mixtures with ingredients for which the approach in 2.8.2.~~3~~.2.2.3.3 does not apply is summarized in Table 2.8.~~2~~3 below.

2.8.2.~~3.~~2.2.3.5 Extreme pH-values

When considering testing of the mixture, classifiers are encouraged to use a tiered weight of evidence approach as included in the criteria for classification of substances for skin corrosion to help ensure an accurate classification, as well as to avoid unnecessary animal testing. In the absence of any other information, a mixture is considered corrosive (Class 8) if it has a pH ≤ 2 or a pH ≥ 11.5. However, if consideration of acid/alkaline reserve[6] suggests the mixture may not be corrosive despite the low or high pH value, this needs to be confirmed by other data, preferably by data from an appropriate validated *in vitro* test. Alternatively the ingredients of the mixture are evaluated and if none of them is classified to class 8, the mixture needs not to be classified as class 8.

2.8.2.~~3~~.2.2.3.~~5~~6 Exemptions

On occasion, reliable data may show that the skin corrosion of an ingredient will not be evident when present at a level above the generic concentration limits/cut-off values mentioned in 2.8.2.~~3~~.2.2.3.3 and Table 2.8.~~2~~3. In these cases the mixture may be classified

[6] *Acid/Alkaline reserve may be determined e.g. by the methodology detailed in Young J.R., How M.J., Walker A.P., Worth W.M.H. (1988): Classification as corrosive or irritant to skin of preparations containing acidic or alkaline substances, without testing on animals. Toxicology in Vitro* ***2****, 19-26 and Young J.R., How M.J. (1994): Product classification as corrosive or irritant by measuring pH and acid/alkali reserve. In Alternative Methods in Toxicology vol. 10 - In Vitro Skin Toxicology: Irritation, Phototoxicity, Sensitization, eds. A.Rougier, A.M. Goldberg and H.I Maibach, Mary Ann Liebert, Inc. 23-27.*

according to those data. On occasion, when it is expected that the skin corrosion of an ingredient will not be evident when present at a level above the generic concentration cut-off values mentioned in 2.8.2.~~3~~.2.2.3.3 and Table 2.8.~~2~~3, testing of the mixture may be considered. In those cases the tiered weight of evidence approach shall be applied as described in 2.8.2.2 and illustrated in Figure 2.8.~~1~~2.

2.8.2.~~3~~.2.2.3.~~6~~.7 If there are data showing that (an) ingredient(s) may be corrosive to skin at a concentration of < 1% (corrosive) the mixture shall be classified accordingly.

Table 2.8.2: Concentration of ingredients of a mixture when the additivity approach does not apply, that would trigger classification of the mixture as corrosive to skin

Ingredient	Concentration	Mixture classified as
Acid with pH ≤ 2	≥ 1%	Class 8
Base with pH ≥ 11.5	≥ 1%	Class 8
Other skin corrosive (Class 8) ingredient	≥ 1%	Class 8

Figure 2.8.2: Tiered evaluation for skin corrosion (mixtures)

Step	Parameter	Finding	Conclusion
1a:	Existing human or animal skin corrosion data [a] → ↓ Not corrosive/No data ↓	Skin corrosive →	Classify as **Class 8** [b]
1b:	Existing human or animal skin corrosion data [a] → ↓ No data/Insufficient data ↓	Not a skin corrosive →	**Not classified as Class 8** [b] **(in case it is not corrosive to metals)**
2:	Other existing skin data in animals [c] → ↓ No/Insufficient data	Yes; other existing data showing that substance may cause skin corrosion →	May be deemed to be a **Class 8** [b]

Figure 2.8.2: Tiered evaluation for skin corrosion (mixtures)

Step	Parameter	Finding	Conclusion
	↓		
3a:	Existing *ex vivo/in vitro* data [d] → ↓ Negative response ↓	Positive on corrosivity: Skin corrosive →	Classify as **Class 8** [b]
3b:	Existing *ex vivo/in vitro* data [e] → ↓ No/insufficient data ↓	Negative response on corrosivity: Not a skin corrosive →	Not classified as Class 8 [b] (in case it is not corrosive to metals)
4a:	Apply "bridging principles" [f] → ↓ No/Insufficient data ↓	Skin corrosive →	Classify as **Class 8** [b]
4b:	Apply "additivity approach" [g] → ↓ No/Insufficient data or not applicable ↓	Skin corrosive →	Classify as **Class 8** [b]
4c:	Apply "Non additivity approach" [h] → ↓ No/Insufficient data or not applicable ↓	Skin corrosive →	Classify as **Class 8** [b]

Figure 2.8.2: Tiered evaluation for skin corrosion (mixtures)			
Step	**Parameter**	**Finding**	**Conclusion**
4d:	pH-based assessment (with consideration of acid/alkaline reserve of the chemical) [i] →	pH ≤ 2 or ≥ 11.5 with high acid/alkaline reserve or no data for acid/alkaline reserve →	Classify as **Class 8**
	↓ Not pH extreme, no pH data or extreme pH with data showing low/no acid/alkaline reserve ↓		
5:	Validated Structure Activity Relationship (SAR) methods →	Skin corrosive →	Deemed to be **Class 8** [b]
	↓ No/Insufficient data ↓		
6:	Consideration of the total weight of evidence [j] →	Skin corrosive →	Deemed to be **Class8** [b]
	↓		
7:	**Not classified as Class 8 (in case it is not corrosive to metals)**		

Toxicology vol. 10 - In Vitro Skin Toxicology: Irritation, Phototoxicity, Sensitization, eds. A.Rougier, A.M. Goldberg and H.I Maibach, Mary Ann Liebert, Inc. 23-27.

[a] *Existing human or animal data could be derived from single or repeated exposure(s), for example in occupational, consumer, transport, or emergency response scenarios; or from purposely-generated data from animal studies conducted according to validated and internationally accepted test methods. Although human data from accident or poison centre databases can provide evidence for classification, absence of incidents is not itself evidence for no classification as exposures are generally unknown or uncertain;*

[b] *Classify in Class 8, as applicable;*

[c] *All existing animal data shall be carefully reviewed to determine if sufficient skin corrosion evidence is available. In evaluating such data, however, the reviewer shall bear in mind that the*

reporting of dermal lesions may be incomplete, testing and observations may be made on a species other than the rabbit, and species may differ in sensitivity in their responses;

[d] *Evidence from studies using validated protocols with isolated human/animal tissues or other, non-tissue-based, though validated, protocols shall be assessed. Examples of internationally accepted, validated test methods for skin corrosion include OECD Test Guideline 430 (Transcutaneous Electrical Resistance Test (TER)), 431 (Human Skin Model Test), and 435 (Membrane Barrier Test Method).*

[e] *In accordance to 2.8.2.2.4.1.4*

[f] *In accordance to 2.8.2.2.2.2*

[g] *In accordance to 2.8.2.2.2.3.2*

[h] *In accordance to 2.8.2.2.2.3.4*

[i] *In accordance to 2.8.2.2.2.3.5. Measurement of pH alone may be adequate, but assessment of acid or alkali reserve (buffering capacity) would be preferable. Presently, there is no validated and internationally accepted method for assessing this parameter;*

[j] *All information that is available shall be considered and an overall determination made on the total weight of evidence. This is especially true when there is conflict in information available on some parameters. Expert judgment shall be exercised prior to making such a determination. Negative results from applicable validated skin corrosion/irritation in vitro tests are considered in the total weight of evidence evaluation.*

2.8.3 Assignment of packing group

2.8.3.1 Substances and mixtures of Class 8 are divided among three packing groups according to their degree of danger in transport as follows:

(a) Packing group I: Very dangerous substances and mixtures;

(b) Packing group II: Substances and mixtures presenting medium danger;

(c) Packing group III: Substances and mixtures presenting minor danger.

2.8.3.2 Allocation of substances and mixtures listed in the Dangerous Goods List in Chapter 3.2 to packing groups in Class 8 has been made on the basis of experience taking into account such additional factors as inhalation risk (see 2.8.1.4) and reactivity with water (including the formation of dangerous decomposition products).

2.8.3.3 Unless otherwise specified in section 2.8.3.4 to 2.8.3.5, substances and mixtures not listed by name in the Dangerous Goods List shall be assigned to packing groups as follows:

~~(a) Substances and mixtures classified as Class 8A are assigned to packing group I~~

~~(b) Substances and mixtures classified as Class 8B are assigned to packing group II~~

~~(c) Substances and mixtures classified as Class 8C are assigned to packing group III~~

~~(d) Substances and mixtures classified as Class 8 without sub-classification are assigned to packing group I.~~

Table 2.8.3 for substances and mixtures not listed by name in the Dangerous Goods List if human data or test data (animal or in vitro) is available

PG I	Corrosive responses in at least one animal following exposure ≤ 3 min during an observation period ≤ 1 h or according to in vitro test results
PG II	Corrosive responses in at least one animal following exposure > 3 min and ≤ 1 h and observations ≤ 14 days h or according to in vitro test results
PG III	Corrosive responses in at least one animal after exposures > 1 h and ≤ 4 h and observations ≤ 14 days h or according to in vitro test results

2.8.3.4 Substances where only an extreme pH-value is available are assigned to packing group I. Substances classified based on validated structure activity relationship (SAR) are assigned to the appropriate packing group. For mixtures the alternative methods are used in this cases as described below.

2.8.3.~~4.~~5 Notwithstanding 2.8.3.3, the packing group of mixtures classified as Class 8A based on additivity calculations (see 2.8.2.~~3~~.2.2.3.2 and 2.8.2.~~3~~.2.2.3.3) may be assigned using the following method:

(a) Derive the packing group for each individual ingredient. For substances listed by name in the Dangerous Goods List, the packing group shall be taken directly from the list. For substances not listed by name, the packing group from the most appropriate n.o.s entry shall be used;

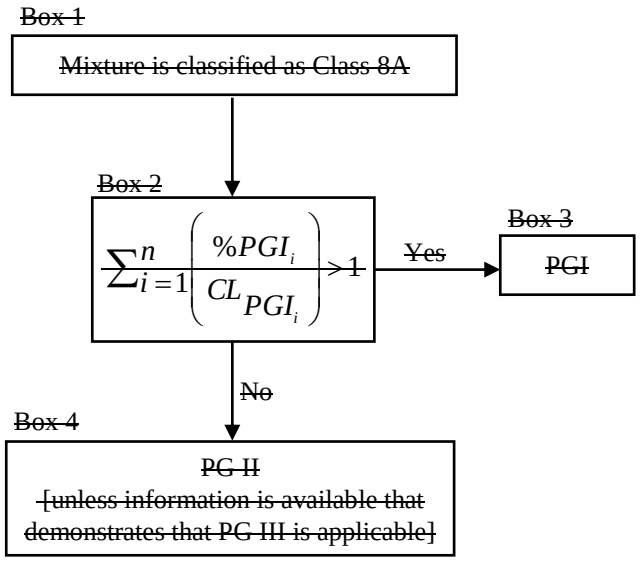
(b) Identify the specific or generic concentration threshold for each individual ingredient. For some substances listed by name on the Dangerous Goods List, the concentration threshold can be taken directly from the list. If no specific concentration threshold is available, generic concentration threshold listed in Table 2.8.~~3~~4 shall be used;

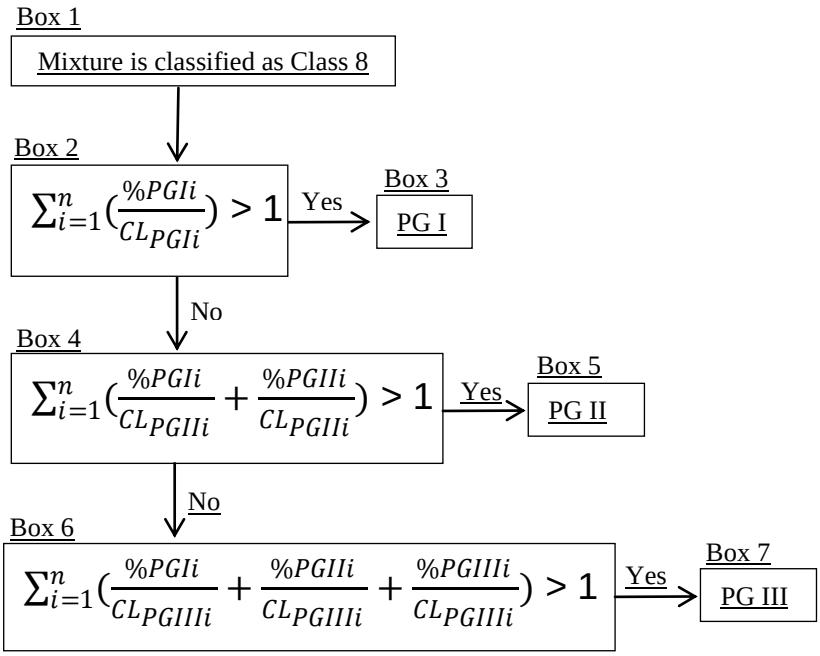
(c) Assign the packing group for the mixture in accordance with Figure 2.8.23 [unless information is available that demonstrates that packing group III is applicable].

Table 2.8.~~3~~4: Generic concentration limit for determination of the packing group of mixtures classified as Class 8A based on additivity calculations

Generic Concentration Limit	Concentration
CL PG I	[50%]
CL PG II	[15%]
CL PG III	[5%]

Figure 2.8.2~~3~~: Flow chart scheme for assignment of packing group for ~~mixtures with hazard classification 8A~~ based on additivity calculations





Notes to Figure 2.8.2~~3~~:

% PG I_i is the concentration of ingredient i assigned to packing group I.

% PG II_i is the concentration of ingredient i assigned to packing group II.

% PG III_i is the concentration of ingredient i assigned to packing group III

$CL_{PG\ Ii}$ is the concentration limit for ingredient i with packing group I. This concentration limit can be either a specific concentration limit from the Dangerous Goods List or generic concentration limit from Table 2.8.~~3~~.4

$CL_{PG\ IIi}$ is the concentration limit for ingredient i with packing group II. This concentration limit can be either a specific concentration limit from the Dangerous Goods List or generic concentration limit from Table 2.8.4.

$CL_{PG\ IIIIi}$ is the concentration limit for ingredient i with packing group III. This concentration limit can be either a specific concentration limit from the Dangerous Goods List or generic concentration limit from Table 2.8.4.

2.8.3.~~5~~6 Notwithstanding 2.8.3.3, the packing group of mixtures classified as Class 8 ~~without sub-~~classification following the non additivity approach or using the extreme pH-value may be assigned using the following method:

(a) Derive the packing group for each individual ingredient. For substances listed by name in the Dangerous Goods List, the packing group shall be taken directly from the list. For substances not listed by name, the packing group from the most appropriate n.o.s entry shall be used;

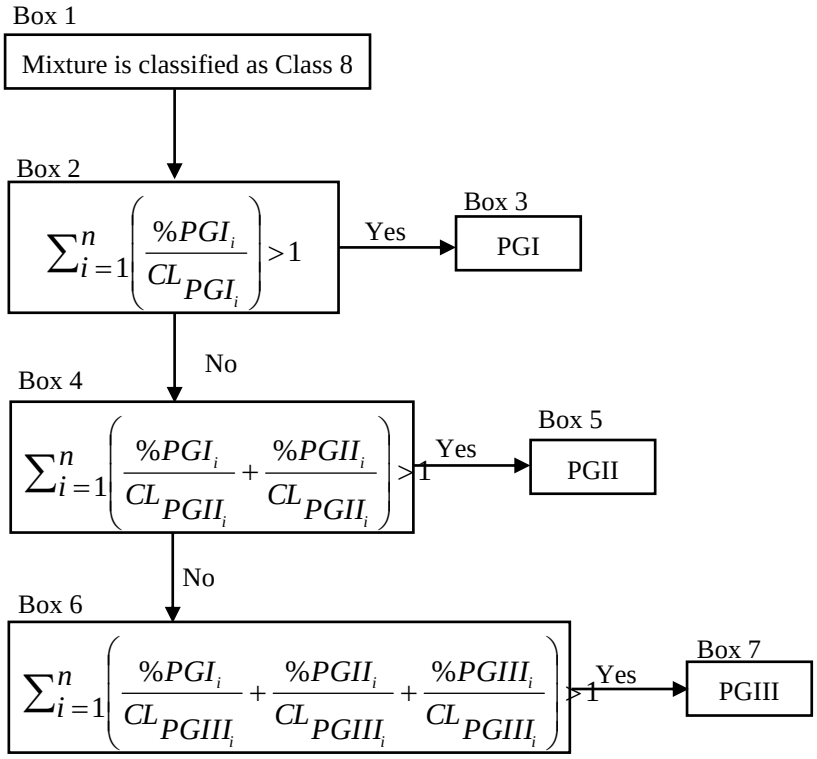
(b) Identify the specific or generic concentration threshold for each individual ingredient. For some substances listed by name on the Dangerous Goods List, the concentration threshold can be taken directly from the list. If no specific concentration threshold is available, generic concentration threshold listed in Table 2.8.4.5 shall be used;

(c) Assign the packing group for the mixture in accordance with Figure 2.8.3.

Table 2.8.4~~5~~: Generic concentration limit for determination of the packing group of mixtures classified as Class 8 ~~without sub-classification~~

Generic Concentration Limit	Concentration
CL PG I	[5%]
CL PG II	[3%]
CL PG III	[1%]

Figure 2.8.~~3~~4: Flow chart scheme for assignment of packing group for mixtures classified as Class 8 ~~without sub-classification~~ based on non-additivity



Notes to Figure 2.8.~~3~~4:

% PG I_i is the concentration of ingredient i assigned to packing group I.

% PG II_i is the concentration of ingredient i assigned to packing group II.

% PG III_i is the concentration of ingredient i assigned to packing group III.

$CL_{PG\ Ii}$ is the concentration limit for ingredient i in PG I. This concentration limit can be either a specific concentration limit taken from the Dangerous Goods List or the generic concentration limit from Table 2.8.~~4~~.5

$CL_{PGI\ Ii}$ is the concentration limit for ingredient i in PG II. This concentration limit can be either a specific concentration limit taken from the Dangerous Goods List or the generic concentration limit from Table 2.8.~~4~~.5

$CL_{PG\ IIIi}$ is the concentration limit for ingredient i in PG III. This concentration limit can be either a specific concentration limit taken from the Dangerous Goods List or the generic concentration limit from Table 2.8.~~4~~.5

2.8.4 Corrosive to metals

2.8.4.1 Liquids, and solids which may become liquid during transport, which are judged not to be corrosive to skin, but which exhibit a corrosion rate on either steel or aluminium surfaces exceeding 6.25 mm a year at a test temperature of 55 °C when tested on both materials are assigned to Class 8.

2.8.4.2 For the purposes of testing steel, type S235JR+CR (1.0037 resp. St 37-2), S275J2G3+CR (1.0144 resp. St 44-3), ISO 3574 or Unified Numbering System (UNS) G10200 or a similar type or SAE 1020, and for testing aluminium, non-clad, types 7075–T6

or AZ5GU-T6 shall be used. An acceptable test is prescribed in the Manual of Tests and Criteria, Part III, Section 37.

NOTE: *Where an initial test on either steel or aluminium indicates the substance being tested is corrosive the follow up test on the other metal is not required.*

2.8.4.3 Packing group III is assigned in accordance with Table 2.8.5.

Table 2.8.5

Packing Group	Effect
III	Corrosion rate on either steel or aluminium surfaces exceeding 6.25 mm a year at a test temperature of 55 ºC when tested on both materials