

Interpolation within one hazard category using in vitro data from a Human Skin Model (HSM) test (OECD TG 431)

This example uses skin corrosion in vitro data from a Human Skin Model (HSM) test (OECD TG 431) to demonstrate the application of the interpolation within one hazard category bridging principle.

OECD TG 431 indicates that the HSM test:

- (i) allows the identification of corrosive substances and mixtures; and
- (ii) enables the identification of non-corrosive substance and mixtures when supported by a weight of evidence determination using other existing information (e.g. pH).

Interpolation within one hazard category

For three mixtures (A, B and C) with identical ingredients, where mixtures A and B have been tested and are in the same corrosion/irritation hazard 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 corrosion/irritation hazard category as A and B (GHS 3.2.3.2.5).

Tested mixture information:

Mixture A – pH (neat liquid): 1.3; Acid reserve: 6.8; Consideration of pH and acid reserve according to Young *et al.* method^{1,2} indicates the mixture may not be corrosive

Mixture B – pH (neat liquid): 1.8; Acid reserve: 2.5; Consideration of pH and acid reserve according to Young *et al.* method^{1,2} indicates the mixture may not be corrosive

| Skin corrosion/irritation classification and test data | | | |
|--|--------------------|---------------------|------------------------|
| Test substance | % Viability 3 mins | % Viability 60 mins | Classification |
| Mixture A | 100 | 30 | Not Skin Cat. 1 |
| positive control | 23 | 12 | |
| Mixture B | 88 | 77 | Not Skin Cat. 1 |
| positive control | 20 | 12 | |

The test substance or mixture is considered to be non-corrosive to skin:

- (i) if the viability after three minutes exposure is $\geq 50\%$ and the viability after 1 hour exposure is $\geq 15\%$.

Mixtures A and B are not classified as Skin Corrosion Category 1 based on test data and consideration of pH/acid reserve.

¹ 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 test on animals. *Toxicology in Vitro* 2, 19-26.

² 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.

Information on ingredients in the tested mixtures:

| Ingredient | Ingredient Skin/Eye classification | Weight % | |
|----------------|------------------------------------|-----------|-----------|
| | | Mixture A | Mixture B |
| Ingredient 1 * | Eye Irritant Category 2 | 25 | 10 |
| Ingredient 2 | Not Classified** | 0.5 | 7 |
| Ingredient 3 | Not Classified** | 2 | 6 |
| Ingredient 4 | Not Classified** | 0.2 | 0.2 |
| Ingredient 5 | Not Classified** | 2 | 2 |
| Water | Not Classified | 70.3 | 74.8 |

* Ingredient 1 is not classified for skin corrosion/irritation based on the results of an OECD TG 404 study

** Not classified for skin corrosion/irritation or serious eye damage/eye irritation based on test data

Untested mixture information:

Mixture C – pH (neat liquid): 1.8; Acid reserve: 3.8; Consideration of pH and acid reserve according to Young *et al.*^{1,2} method indicates the mixture may not be corrosive

| Ingredient | Weight % | | |
|--------------|-----------|-----------|-----------|
| | Mixture A | Mixture C | Mixture B |
| Ingredient 1 | 25 | 15 | 10 |
| Ingredient 2 | 0.5 | 5.6 | 7 |
| Ingredient 3 | 2 | 6 | 6 |
| Ingredient 4 | 0.2 | 0.2 | 0.2 |
| Ingredient 5 | 2 | 2 | 2 |
| Water | 70.3 | 71.2 | 74.8 |

NOTE: In Chapter 1.3 Classification of Hazardous Substances and Mixtures, the principle that the GHS itself does not include requirements for testing substances or mixtures is clearly stated. However, the GHS also recognizes that some parts of regulatory systems (e.g., pesticides) may require data to be generated. In reviewing this example there were different interpretations on whether negative in vitro data in combination with $pH \leq 2$ could be used to justify not being classified as a Skin corrosion Category 1. Where a competent authority requires additional test data, testing and classification should be undertaken in accordance with the competent authority's requirements.

Answer:

Applying the Interpolation within one hazard category bridging principle, the untested Mixture C is not classified as Skin Corrosion Category 1 based on test data of Mixtures A and B and consideration of pH/acid reserve.

Further information and evaluation will be required to determine the classification of untested Mixture C regarding Skin Irritation.

The classification of Mixture C is Serious Eye Damage Category 1.

Rationale:

- Classification via application of substance criteria is not possible since skin corrosion/irritation test data was not provided for the untested mixture;
- Classification via the application of bridging principles can be considered since there are sufficient data on both the individual ingredients and similar tested mixtures;
- 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 hazard category bridging principle can be applied because:
- (i) Mixtures A and B have both been tested and are in the same corrosion/irritation hazard category (i.e. Not classified as Skin Corrosion Category 1); AND
 - (ii) Untested mixture C has the same toxicologically active ingredient (i.e. Ingredient 1) as tested mixtures A and B; AND
 - (iii) The concentration of ingredient 1 in mixture C is intermediate to the concentration of ingredient 1 in mixtures A and B.
- (e) Classification of the mixture based on ingredient information should be considered for serious eye damage/eye irritation (GHS paragraph 3.3.3.1.2).
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(Ref.Doc: ST/SG/AC.10/C.4/2012/25, Annex 2 as amended by INF.35 (24th session))