

Example on 'Permitted Variations' Bridging Principle using Expert Judgement for non-hazardous mixtures

According to section 1.6.3.2.6 in the ECHA Guidance on the application of CLP criteria, a new evaluation of a change in composition of mixtures **not** classified for a specific hazard has to be carried out even if the change is only minor and within the limits of Table 1.2 of Part 1 of Annex I to CLP, because a concentration threshold might be reached and the changed mixture need to be classified as hazardous.

Only increases of the initial concentration of hazardous ingredients in non-hazardous mixtures within the limits of Table 1.2 have to undergo a new review. Indeed an increase in the level of hazard is not expected if the concentration of hazardous substances is decreasing.

The example below covers **only** the endpoint skin. The endpoint eye is not considered.

Note: The principle of permitted variation is endpoint specific. For example, an increase of an ingredient classified for eye and skin effects in a mixture classified only for eye would trigger a new evaluation for classification regards skin effects.

Ingredient	Skin/Eye Classification	Mixture A tested	Tolerance band for changes	Mixture B untested
Non-ionic surfactant P*	Eye Cat 1	6.0 %	4.8 – 7.2	6.0 %
Anionic surfactant K**	Skin Cat 2 Eye Cat 1	10.2 %	9.2 – 11.2	11.1%
Citrate	Not classified	5.0 %	not applicable	6.0 %
Ethanol	Eye Cat 2	4.0 %	3.2 – 4.8	4.5 %
Polycarboxylate	Not classified	0.75 %	not applicable	0.8 %
Water		to 100		to 100
		Skin: not classified OECD 439: EpiSkin™		Skin: not classified

The untested Mixture B does not contain any ingredients classified as Skin Corrosion Cat. 1 and is not extreme pH, consequently, it is not classified as Skin Corrosion Cat. 1.

Mixture A was tested using an *in vitro* Skin Irritation: Reconstructed Human Epidermis ModelEpiSkin™ skin irritation (OECD TG 439). Cell viability was measured by enzymatic conversion of the vital dye MTT into a blue formazan salt that is quantitatively measured after extraction from tissues. Irritant chemicals or mixtures are identified by their ability to decrease cell viability below or equal to 50% for classification as Skin Cat 2.

*D-Glucopyranose, oligomeric, decyl octyl glycosides, CAS No. 68515-73-1

**Benzenesulfonic acid, C10-13-alkyl derivs., sodium salts, CAS No. 68411-30-11

Results for Mixture A

Classification of irritation potential is based upon relative mean tissue viability following the 15 minute exposure period followed by the 42 hour post-exposure.

Mixture A is not a MTT direct reducer.

	Mean OD ₅₄₀ of triplicate tissues	± Standard deviation (SD)	Relative mean tissue viability (%)	± SD of relative mean tissue viability (%)
Negative Control	1.765	0.152	100	8.6
Positive control	0.021	0.003	1.2	0.2
Mixture A	1.546	0.108	87.6	6.1

Quality criteria: The quality criteria for acceptance of the test were satisfied.

Conclusion

Mixture A was tested for its skin irritation potential in an OECD 439 study using EpiSkin™. The tissue viability was 87.6% and is thus clearly above the threshold for classification as Skin Cat 2 of 50%. Therefore Mixture A is not classified as irritant to skin.

Applying the bridging principle 'Permitted variations' with Expert Judgement, the untested Mixture B is not classified for skin irritation/corrosion based on test data available for the Mixture A.

Rationale:

- (a) Mixture A and Mixture B have comparable pH values which are in the following range $2 < \text{pH} < 11.5$
- (b) Mixture A and B contain the same hazardous ingredients.
- (c) Only surfactant K is relevant to the endpoint skin. The amount of surfactant K is higher in Mixture B compared to Mixture A but still within the range of permitted variations.
- (d) Using Expert Judgement, it can be concluded that the increase of surfactant K by 0,9% only in untested Mixture B is not sufficient to significantly change the skin irritation potential compared to Mixture A¹.
- (e) Test data for Mixture A are not close to the threshold for classification as Skin Cat 2.
- (f) Consequently Mixture B is not classified for skin irritation based on test data available for Mixture A.

¹ Rationale used here as a basis for the Expert Judgement: The tissue viability was 87.6% and is thus clearly above the threshold for classification as Skin Cat 2 of 50%. Therefore Mixture A is not classified as irritant to skin. Increase of only 0.9% surfactant will not suffice to reach classification threshold.