



Detergent Industry Network for CLP Classification

RECORD	
Skin/Eye Hazard Classification of Laundry/Home Care Products	
GENERAL INFORMATION	
Company	Company X
Mixture Name	Hand Dish Washing Liquid X
Product category	Hand Dish Washing Liquid Detergent
Mixture number	HDW001
PHYSICAL/ CHEMICAL PROPERTIES	
Physical form	Liquid
pH ¹	5.5
Acid / Alkaline reserve ²	Not needed since pH is not extreme
Other relevant information ³	Young et al.: no data
CLASSIFICATION	
Classification according to CLP criteria (skin/eye hazards)	Skin: Not classified as hazardous to skin CLASSIFICATION Eye: Eye Irritation Cat. 2
Method used to derive Classification	Skin: Weight of Evidence with Expert Judgement Eye: Weight of Evidence with Expert Judgement
APPROVAL	
Classification derived by	J. Doe
Classification completed	2017-02-28
Classification logged on DetNet website	2017-02-28
Classification logging number	DetNet/1234 (logging number as an example only)

1. neat liquid or 10% solution powders

2. Young et al method; expressed as grams NaOH [equivalent] per 100g test material

3. e.g. result of Young et al method calculation if applicable

Supporting Data / Justification Skin

- No skin data are available on the new mixture HDW001 to be classified. Assessment of a new mixture by expert judgment based on the weight of evidence considering existing toxicological information on tested mixtures and data on individual ingredients.
- The pH of the new mixture HDW001 is in the range: $2 < \text{pH} < 11.5$; therefore the pH is not extreme and no need to determine the alkali reserve of the new mixture.
- The new mixture HDW001 does not contain any ingredients classified as Skin Corrosive Cat. 1 thus the new mixture is not Skin Corrosive Cat. 1

To assess classification on skin, a tested mixture was identified and compared with new mixture. The "Tested Mixture example 4" was tested for skin irritancy using an in vitro assay (OECD TG 439, Episkin) with the result "not classified as hazardous on skin".

The tested mixture contains a higher amount of surfactants (18.5 %) than the new mixture HDW001 (16%). The ratio between anionic, amphoteric and non-ionic surfactants is in the same range.

The anionic surfactant content (Benzenesulfonic acid, C10-13-alkyl derivs., sodium salts) in the new mixture has a lower level (10%) than the tested mixture (11%).

The amphoteric surfactant content (1-Propanaminium, 3-amino-N-(carboxymethyl)-N,N-dimethyl-, N-coco acyl derivs., hydroxides, inner salts) in the new mixture has a lower level (3 %) than in the tested mixture (4%).

The non-ionic surfactant content (3 % of Fatty Alcohol (C14-15) ethoxylate 7EO) in the new mixture has a lower level than the tested mixture (3.5 % of Fatty Alcohol (C12-18) ethoxylate 7EO). Both surfactants do not contribute to skin irritation.

- Other ingredients are not expected to influence the classification since they are either at a low level and/or not classified.
- Taking all the information into account, by weight of evidence it can be concluded that the new and the tested mixture are similar enough to allocate the classification of the "Tested Mixture example 4" to the untested mixture HDW001. In conclusion, the new mixture should have same classification as the tested mixture, being "not classified as hazardous on skin".

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Example 4 Mixture Comparison Chart Skin

ID	Ingredient	CAS numbers	Skin Classification	Untested Mixture	TM Example 4
Anionic surfactant					
1015	Benzenesulfonic acid, C10-13-alkyl derivs., sodium salts	68411-30-3	Skin Irritation Cat. 2	10	11
Nonionic surfactant					
1019	Fatty Alcohol (C12-18) ethoxylate 7EO	68213-23-0	Not classified as hazardous to skin	0	3.5
1016	Fatty Alcohol (C14-15) Ethoxylate 7EO	64425-86-1	Not classified as hazardous to skin	3	0
Amphoteric surfactant					
94	1-Propanaminium, 3-amino-N-(carboxymethyl)-N,N-dimethyl-, N-coco acyl derivs., hydroxides, inner salts	61789-40-0	Skin Irritation Cat. 2	3	4
Alcohol/ Solvent					
286	Ethanol	64-17-5	Not classified as hazardous to skin	1	5
Processing Aid					
301	Sodium chloride	7647-14-5	Not classified as hazardous to skin	3	2
Builder					
243	Trisodium citrate	68-04-2	Not classified as hazardous to skin	0.5	0.5
Perfume					
2221	Perfume (not classified for skin & eye)	n.a.	Not classified as hazardous to skin	0.25	0.25
Preservative					
3258	Preservative NOS	n.a.	Not classified as hazardous to skin	0.15	0.15
Minor					
409	Dye (not classified for skin & eye)	n.a.	Not classified as hazardous to skin	0.05	0.05
1029	Water	7732-18-5	Not classified as hazardous to skin	79.05	73.55

Summary of data for TM example 4:

Product Form: Liquid	Product Category: Hand Dish Wash liquid
pH: 6	Acid/Alkaline Reserve: 0
Skin Classification: Not classified as hazardous to skin AISE_example4_summary_OECD_TG_439.pdf	Eye Classification: Eye Irritation Cat. 2 AISE_example4_summary_OECD_TG_438.histopath.pdf AISE_example4_summary_OECD_TG_437.pdf AISE_example4_summary_LVET.pdf

Supporting Data / Justification Eye

- No eye data are available on the new mixture HDW001 to be classified. Assessment of a new mixture by expert judgment based on the weight of evidence considering existing toxicological information on tested mixtures and data on individual ingredients.
- The pH of the new mixture HDW001 is in the range: $2 < \text{pH} < 11.5$; therefore the pH is not extreme and no need to determine the alkali reserve of the new mixture.

“Tested Mixture example 4” was tested for eye irritation using the OECD TG 492 (EpiOcular™ Eye Irritation Test (EIT)), OECD TG 438 (Isolated Chicken Eye plus histopathology) and OECD TG 437 (Bovine Corneal Opacity and Permeability Test).

Neither of the three in-vitro-tests had identified the “Tested Mixture example 4” to be Eye Corrosion Cat. 1 or not classified as hazardous to eyes.

The rationale for classifying the “Tested Mixture Example 4” as Eye Irritation Cat. 2 by expert judgement is based on the weight of evidence, considering the three in-vitro tests, market observation and review of incidents reported to poison control centres. Supporting human data derived from incidents reported to poison control centers have been collected over a 12 month period for the assessment of effects in eyes, e.g. no effects more than minor had been identified for Hand Dishwash Liquids in the MAGAM II study (see below).

On “Tested Mixture Example 4” company owned data have been collected over a 24 month period for the assessment of effects in eyes, displaying 9 cases of mild to moderate irritation (see below).

- The tested mixture “Tested Mixture Example 42 contains a higher amount of surfactants (18.5 %) than the new mixture HDW001 (16%). The ratio between anionic, amphoteric and non-ionic surfactants is in the same range. All surfactants are classified as Eye Corrosion Cat. 1.

The anionic surfactant content (Benzenesulfonic acid, C10-13-alkyl derivs., sodium salts) in the new mixture has a lower level (10%) than the tested mixture (11%).

The amphoteric surfactant content (1-Propanaminium, 3-amino-N-(carboxymethyl)-N,N-dimethyl-, N-coco acyl derivs., hydroxides, inner salts) in the new mixture has a lower level (3 %) than in the tested mixture (4%).

The non-ionic surfactant content (3 % of Fatty Alcohol (C14-15) ethoxylate 7EO) in the new mixture has a lower level than the tested mixture (3.5 % of Fatty Alcohol (C12-18) ethoxylate 7EO).

The alcohol ethoxylates employed in the new and tested mixture have different C-chain length distribution, but the degree of ethoxylation is very similar. The irritation potential of the different alcohol ethoxylates contained in the new and the tested mixture is comparable. Rationale: Most alcohol ethoxylates tested are considered to be moderately to severely irritating. According to the HERA Risk Assessment on Alcohol Ethoxylates (2009) the irritation potential of alcohol ethoxylates does not depend on the C-chain distribution or ethoxylation grade. The severity of eye irritation caused by alcohol ethoxylates was shown to be solely concentration dependent. The alcohol ethoxylates covered by the HERA assessment were in the range of C9 to C19 with 2.5 to 15 ethoxy units. (HERA Risk Assessment, Alcohol Ethoxylates, 2009).

- In the „Tested Mixture Example 4” ethanol is present at 5%, exceeding 1% only in the new mixture HDW001.
- Other ingredients are not expected to influence the classification since they are either at a low level and/or not classified.
- Taking all the information into account, by expert judgement considering the weight of evidence summarised below it can be concluded that the new and the tested mixture are similar enough to allocate the classification of the “Tested Mixture example 4” to the new mixture HDW001. In conclusion, the new mixture HDW001 should have same classification as the „Tested Mixture example 4”, being Eye Irritation Cat. 2”.

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Example 4 Mixture Comparison Chart Eye

ID	Ingredient	CAS numbers	Eye Classification	Untested Mixture	TM Example 4
Anionic surfactant					
1015	Benzenesulfonic acid, C10-13-alkyl derivs., sodium salts	68411-30-3	Serious Eye Damage Cat. 1	10	11
Nonionic surfactant					
1019	Fatty Alcohol (C12-18) ethoxylate 7EO	68213-23-0	Serious Eye Damage Cat. 1	0	3.5
1016	Fatty Alcohol (C14-15) Ethoxylate 7EO	64425-86-1	Serious Eye Damage Cat. 1	3	0
Amphoteric surfactant					
94	1-Propanaminium, 3-amino-N-(carboxymethyl)-N,N-dimethyl-, N-coco acyl derivs., hydroxides, inner salts	61789-40-0	Serious Eye Damage Cat. 1	3	4
Alcohol/ Solvent					
286	Ethanol	64-17-5	Eye Irritation Cat. 2	1	5
Processing Aid					
301	Sodium chloride	7647-14-5	Not classified as hazardous to eyes	3	2
Builder					
243	Trisodium citrate	68-04-2	Not classified as hazardous to eyes	0.5	0.5
Perfume					
2221	Perfume (not classified for skin & eye)	n.a.	Not classified as hazardous to eyes	0.25	0.25
Preservative					
3258	Preservative NOS	n.a.	Serious Eye Damage Cat. 1	0.15	0.15
Minor					
409	Dye (not classified for skin & eye)	n.a.	Not classified as hazardous to eyes	0.05	0.05
1029	Water	7732-18-5	Not classified as hazardous to eyes	79.05	73.55

Summary of data for TM example 4:

Product Form: Liquid	Product Category: Hand Dish Wash liquid
pH: 6	Acid/Alkaline Reserve: 0
Skin Classification: Not classified as hazardous to skin AISE_example4_summary_OECD_TG_439.pdf	Eye Classification: Eye Irritation Cat. 2 AISE_example4_summary_OECD_TG_438.histopath.pdf AISE_example4_summary_OECD_TG_437.pdf AISE_example4_summary_OECD_TG_492.pdf

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Example 4: Weight of evidence analyses for classification of HDW001 for effects on eyes (use of testing and non-testing methods)

	Full Reference	Study result	Data quality Klimisch score	Adequacy and relevance	Coverage of relevant parameters/ observations Yes/No	Consistency	Conclusive remark
Existing human data on company-owned mixtures similar to HDW001	PCC data collected over a 24 months period	<p>9 cases of mild to moderate eye effects only were reported out of all sold products*. In the cases where follow-up information was available, all ocular effects were fully reversible within a few days.</p> <p><i>*This is an example, in reality the number of cases will need to be identified relative to the number of products sold in a specific geographical area.</i></p>	Not applicable to PCC data as Klimisch score is applicable to assessing the reliability of toxicological studies.	Supportive information. Limitation due to unknown dose and exposure duration. No CLP criteria for C&L based on human data.	No, not in every case all relevant parameters are covered (e.g. exposure conditions, detailed tissue effects).	Consistent with existing <i>in vitro</i> studies and other human experience, which identify the hand dish washing liquid HDW001 as not Cat. 1	Supportive data.
Existing human data on similar mixtures	MAGAM II Multicentre multi-national prospective, study of human eye exposures reported to Poisons Control Centres (PCCs), over a 24 months period (data collection from 6 to 18 months per PCC).	28 reported cases related to hand dish washing liquids: mild to moderate but no severe eye irritation after exposure. In the cases where follow-up information was available, all ocular effects were fully reversible within a few days.	Not applicable to PCC data as Klimisch score is applicable to assessing the reliability of toxicological studies.	Supportive information. Scoring based on PCC severity scoring system complemented by MAGAM reported symptoms. No CLP criteria for C&L based on human data. Information provided as a product category containing different products vs an individual named product.	Although not in every case all relevant parameters are available (e.g. exposure conditions), tissue observations are conducted typically by an ophthalmologist and reported in a standardized way.	Consistent with existing <i>in vivo</i> and <i>in vitro</i> studies, which identify the hand dish washing liquid HDW001 as not Cat. 1	Supportive data.

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<p><i>In vitro</i> data on eye irritation corrosion</p>	<p>Isolated Chicken Eye Test OECD 438 with histopathology as an additional endpoint, 2015</p>	<p>No Prediction can be Made based on a combination of the endpoint categories of II;II;III. This combination of endpoint categories is much lower than those used to identify classification as Cat. 1.</p> <p>Not Cat. 1 based on criteria developed by Cazelle et al. (2014) for histopathological evaluation of non-pH-extreme detergents and cleaning products.</p>	<p>1</p>	<p>Key study conducted according to GLP. Due to histopathology, severity and persistence of effects are covered.</p>	<p>Yes</p>	<p>Consistent with existing <i>in vitro</i> studies and human experience data which identify the hand dish washing liquid HDW001 as not Cat. 1</p>	<p>Key data. OECD 438 study with histopathology as an additional endpoint.</p>
<p><i>In vitro</i> data on eye irritation corrosion</p>	<p>Reconstructed human Cornea-like Epithelium (RhCE) Test Method OECD 492, 2016</p>	<p>Tissue viability in the EpiOcular™ EIT was 45 %, identifying that the mixture requires classification for effect on eyes</p>	<p>1</p>	<p>Key study conducted according to GLP. Study allows judgement on need or no need for classification. OECD 492 allows discrimination between materials not requiring classification from those requiring classification (Cat. 2/ Cat. 1).</p>	<p>Yes</p>	<p>Consistent with existing <i>in vitro</i> studies and human experience data</p>	<p>Key data.</p>
<p><i>In vitro</i> data on eye irritation corrosion</p>	<p>Bovine Corneal Opacity and Permeability Test OECD 437, 2015</p>	<p>No Prediction can be Made based on <i>In Vitro</i> Irritancy Score (IVIS) of 10.3. The IVIS is far below the threshold of 55.1 for classification as Cat. 1</p>	<p>1</p>	<p>Key study conducted according to GLP. Study allows judgement on severity of effects but not persistence of effects and it does not allow identification of Cat. 2 specifically.</p>	<p>Yes</p>	<p>Consistent with existing <i>in vitro</i> studies and human experience data</p>	<p>Key data.</p>

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<i>In vitro</i> data on skin irritation	<i>In Vitro</i> Skin Irritation: Reconstructed Human Epidermis (RHE) Test Method OECD 439, 2014	Tissue viability in EpiSkin™ test method was 75 %, identifying that the tested mixture does not require classification for skin irritation.	1	Study confirms low skin irritation potential.	Yes	Consistent with <i>existing in vitro</i> studies and human experience data	Supportive data. Effects on skin except for skin corrosion do not allow assessment for effects on eyes.
Physico-chemical properties	Determination of pH, acidity and alkalinity measurement according to OECD 122	pH is 6.0, HDW001 is therefore not pH-extreme	1	Supportive information because pH alone does not allow assessment of the eye irritancy.	Yes		Supportive data.
Overall conclusion	<p>Human data indicates only mild to moderate and fully reversible effects.</p> <p><i>In vitro</i> data indicates classification required but not Cat. 1 classification.</p> <p>pH and skin effects do not indicate corrosive effects.</p> <p>In conclusion, a WoE evaluation of the consistency, quality and relevance of all available data allows a decision on the eye irritation/serious eye damage potential of the Hand Dish Washing Liquid HDW001. The Hand Dish Washing Liquid HDW001 should be classified as eye Irritant UN GHS Cat. 2.</p>						

Remark: This example has been developed only to illustrate how the classification of an untested mixture could be derived and justified. This does not contain any recommendation for a testing strategy. However, the BCOP has very recently been included in a testing strategy for antimicrobial cleaning products (AMCPs) under the U.S. EPA classification and labeling system (Clippinger et al, ALTEX 33(4), 2016).