

CLH report

Proposal for Harmonised Classification and Labelling

Based on Regulation (EC) No 1272/2008 (CLP Regulation),
Annex VI, Part 2

Substance Name:

**3,3'-dicyclohexyl-1,1'-methylenebis(4,1-phenylene)diurea
(Complex soap TH 28)**

EC Number: 406-370-3
CAS Number: 58890-25-8
Index Number: 616-094-00-7

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Part A.

1 PROPOSAL FOR HARMONISED CLASSIFICATION AND LABELLING

1.1 Substance

The table below shows identity information for substance Complex soap TH 28.

Table 1: Substance identity

Substance name:	Complex soap TH 28
Chemical name:	3,3'-dicyclohexyl-1,1'-methylenebis(4,1-phenylene)diurea
EC number:	406-370-3
CAS number:	58890-25-8
Annex VI Index number:	616-094-00-7
Degree of purity:	> 95 ≤ 100 % (w/w)
Impurities:	Impurities are not considered relevant for the classification and labelling of the substance.

1.2 Harmonised classification and labelling proposal

Table 2: The current Annex VI entry and the proposed harmonised classification

	Regulation 1272/2008/EC (CLP)
Current entry in Annex VI, CLP Regulation	Skin Sens. 1, H317 Aquatic Chronic 4, H413
Current proposal for consideration by RAC	Removal of: Skin Sens. 1, H317 Aquatic Chronic 4, H413
Resulting harmonised classification (future entry in Annex VI, CLP Regulation)	No classification.

1.3 Proposed harmonised classification and labelling based on CLP Regulation

Table 3: Proposed classification according to the CLP Regulation

CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification ¹⁾	Reason for no classification ²⁾
2.1.	Explosives				Hazard class not assessed in this dossier
2.2.	Flammable gases				Hazard class not assessed in this dossier
2.3.	Flammable aerosols				Hazard class not assessed in this dossier
2.4.	Oxidising gases				Hazard class not assessed in this dossier
2.5.	Gases under pressure				Hazard class not assessed in this dossier
2.6.	Flammable liquids				Hazard class not assessed in this dossier
2.7.	Flammable solids				Hazard class not assessed in this dossier
2.8.	Self-reactive substances and mixtures				Hazard class not assessed in this dossier
2.9.	Pyrophoric liquids				Hazard class not assessed in this dossier
2.10.	Pyrophoric solids				Hazard class not assessed in this dossier
2.11.	Self-heating substances and mixtures				Hazard class not assessed in this dossier
2.12.	Substances and mixtures which in contact with water emit flammable gases				Hazard class not assessed in this dossier
2.13.	Oxidising liquids				Hazard class not assessed in this dossier
2.14.	Oxidising solids				Hazard class not assessed in this dossier
2.15.	Organic peroxides				Hazard class not assessed in this dossier
2.16.	Substance and mixtures corrosive to metals				Hazard class not assessed in this dossier
3.1.	Acute toxicity - oral				Hazard class not assessed in this dossier
	Acute toxicity - dermal				Hazard class not assessed in this dossier
	Acute toxicity - inhalation				Hazard class not assessed in this dossier
3.2.	Skin corrosion / irritation				Hazard class not assessed in this dossier
3.3.	Serious eye damage / eye irritation				Hazard class not assessed in this dossier
3.4.	Respiratory sensitisation				Data lacking and hazard class not assessed in this dossier
3.4.	Skin sensitisation	none		Skin Sens. 1, H317	new data, negative mLLNA
3.5.	Germ cell mutagenicity				Hazard class not assessed in this dossier
3.6.	Carcinogenicity				Hazard class not assessed in this dossier
3.7.	Reproductive toxicity				Hazard class not assessed in this dossier
3.8.	Specific target organ toxicity –single exposure				Hazard class not assessed in this dossier
3.9.	Specific target organ toxicity – repeated exposure				Hazard class not assessed in this dossier

CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification ¹⁾	Reason for no classification ²⁾
3.10.	Aspiration hazard				Hazard class not assessed in this dossier
4.1.	Hazardous to the aquatic environment	none		Aquatic Chronic 4, H413	new data
5.1.	Hazardous to the ozone layer				Hazard class not assessed in this dossier

¹⁾ Including specific concentration limits (SCLs) and M-factors

²⁾ Data lacking, inconclusive, or conclusive but not sufficient for classification

Labelling: none

2 BACKGROUND TO THE CLH PROPOSAL

3,3'-dicyclohexyl-1,1'-methylenebis(4,1-phenylene)diurea (Complex soap TH 28) is an industrial chemical in the meaning of REACH Regulation (EC 1907/2006). The substance has an existing harmonised classification according to Regulation 1272/2008/EC (CLP), Annex VI for the hazard classes: skin sensitisation and environmental hazard. However the presence of new data from the REACH registration showed the need to revise the current classification. This CLH proposal aims to revoke the classification and labelling of Complex soap TH 28 as Skin Sens. 1 (H317) and Aquatic Chronic 4 (H413).

2.1 History of the previous classification and labelling

Complex soap TH 28 was primarily classified and labelled with Xi; R43, 53, S24, 37, 61 and adopted into Annex I of Directive 67/548/EEC with the 29th ATP by the authorities.

With implementation of the CLP Regulation the substance was classified and labelled with Skin Sens. 1 (H317) and Aquatic Chronic 4 (H413).

Data from the REACH registration dossiers were taken as a basis for this CLH proposal.

The CLH dossier submitter registered Complex soap TH 28 according to REACH Regulation Annex VII. Previously, Complex soap TH 28 has been notified by three companies under the new substances regulation in accordance with Directive 92/32/EEC (NONS; Council Directive 92/32/EEC of April 1992 amending for the seventh time Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances. O.J.No L 154, 5.6.1992, p.1). Information from these former notifications was made available by ECHA for several endpoints, as data was submitted at least 12 years ago. Endpoints included were:

- 7.2 Melting/freezing point
- 7.4 Relative density
- 7.5 Vapour pressure
- 7.6 Surface tension
- 7.8 Partition coefficient n-octanol/water
- 7.11 Explosive properties
- 7.12 Self-ignition temperature
- 8.5.1 Acute toxicity: oral
- 8.5.3 Acute toxicity: dermal
- 8.6.1 Short-term repeated toxicity study (28 days)
- 8.8.1 Assessment of toxicokinetic behaviour
- 9.1.1 Short-term toxicity testing on invertebrates
- 9.1.2 Growth inhibition study aquatic plants
- 9.1.3 Short-term toxicity testing on fish
- 9.1.4 Activated sludge respiration inhibition testing
- 9.2.1.1 Ready biodegradability

According to Article 10 and 25(3) of the REACH Regulation the CLH dossier submitter made use of the study summaries and robust study summaries applicable for Annex VII REACH registration. The CLH dossier submitter respected the property rights and possible confidentiality of the study summaries and robust study summaries and used them only for the purpose of registration. Further, the CLH dossier submitter followed Article 11 and Article 26(3) of the REACH Regulation.

New data of substance specific properties and of required endpoints not available from former notifications was generated, including:

7.3 Boiling point

7.7 Water solubility

7.10 Flammability

8.1 Skin irritation / corrosion

8.2 Eye irritation

8.3 Skin sensitisation

8.4 Genetic toxicity in vitro

9.1.3 Growth inhibition study aquatic plants.

Based on the study results available from former notifications and new data generated, specifically, the new data according to REACH Regulation, Annex VII section 8.3 and 9.1.2 shows that Complex soap TH 28 has no skin sensitising potential and is not toxic to the aquatic environment. A revoke of the current classification is justified.

Notably, Complex soap TH 28 has not been tested for skin sensitisation before. The current classification and labelling as Skin Sens.1 (H317) may have been based on its impurities, e.g. residual amine (details are not available to applicant) which one of them is a potent skin sensitizer and has a harmonised classification according to Annex VI of CLP. The presence of significant residual amine in batches of former notifications was confirmed by the reported vapour pressure (111 Pa at 25 °C which is related to the residual amine vs. 0.35 at 25 °C for the pure substance, as calculated and expected for such a structure, see section 4.6 of the IUCLID dossier). However, the effects of potential impurities e.g. due to different synthesis conditions, have to be assessed separately from the effects noted of the “pure” registered substance as the substance was tested as produced.

The new information presented was generated using the registered substance and results clearly show that classification and labelling of pure Complex soap TH 28 as Skin Sens.1 (H317) is not justified.

2.2 Short summary of the scientific justification for the CLH proposal

A revoke of the classification of Complex soap TH 28 as skin sensitizer and for its chronic aquatic effects is proposed. Based on the available/presented new data from the REACH registration dossier the classification/labelling with Skin Sens. 1 (H317) and Aquatic Chronic 4 (H413) is deemed to be not justified.

Skin sensitisation

Data from a mouse Local Lymph Node Assay (LLNA) performed in 2009 are available for Complex soap TH 28 (purity > 95 %). The skin sensitisation potential of Complex soap TH 28 was tested in a LLNA performed in CBA/J@Rj mice, according to OECD Guideline 429 and EU Method B.42. Results from this study have shown that Complex soap TH 28 with a purity of > 95 % does not reveal skin sensitisation potential according to criteria of CLP Regulation.

In the main study sixteen female CBA/J@Rj mice were randomly assigned to four groups. Three groups were treated with Complex soap TH 28 at concentrations of 10 %, 5 % and 2.5 %. The control group was treated with pure vehicle acetone:olive oil (4:1, v/v; AOO). The test item solutions were applied on the dorsal surface of ears of the animals (25 µL/ear) for three consecutive days (days 1, 2 and 3). After application of the 10 % and 5 % test item solutions on ears of animals, a precipitate on the treatment area was observed. There was no treatment on days 4, 5 and 6. On day 6, the cell proliferation in local lymph nodes was determined by measuring the incorporation of

tritiated methyl thymidine ($^3\text{HTdR}$). The values obtained from analysis were used to calculate stimulation indices (SI).

No mortality or systemic clinical signs were observed during the study. No treatment related effect on body weight was observed. Additionally, no irritation or other local effects were observed. Stimulation index values of the test item were 0.5, 0.5 and 0.7 at treatment concentrations of 10 %, 5 % and 2.5 %, respectively. Thus, no SI value of 3 or more was noted and further, there was no dose-related response, which indicates a negative result in this test system.

The results of a reliability check (performed within an interval of no longer than six months), demonstrated the appropriate performance of the assay in accordance with the OECD Guideline 429. The positive control substance α -Hexylcinnamaldehyde (HCA, CAS 101-86-0) was examined at a concentration of 25 % in the vehicle AOO. A significant proliferation of lymphocytes in the lymph nodes draining the site of the test substance application was noted for HCA with a SI value of 4.9, which is ≥ 3 and confirms the validity of the LLNA in the performing laboratory.

Complex soap TH 28 did not reveal a skin sensitisation potential in mice of this LLNA test according to OECD Guideline 429 and EU Method B.42. Overall, the registered compound Complex soap TH 28 is not considered as a substance that can lead to sensitisation following skin contact taking into account to CLP criteria. Therefore, current classification and labelling according to CLP Regulation with Skin Sens. 1, H317 is proposed to be removed.

Aquatic toxicity

Water Solubility (new study)

The new information about the water solubility of Complex soap TH 28 is regarded as important for current classification and labelling although the method applied was not substance specific and could not be used for to determine the real concentration of the aquatic toxicity tests.

The water solubility of Complex soap TH 28 was determined according to EU method B.6 and OECD guideline 106 using the shake flask method (LAB Research Ltd. (2010a)). As there is no GC- or HPLC-method available for the test item, the dissolved organic carbon (DOC) content of a saturated solution was determined resulting in 3.23 mg/L.

As this represents the result obtained for the DOC part, the water solubility was recalculated for Complex soap TH 28 as such, resulting in a water solubility of 4.47 mg/L based on the carbon content of 72.3 %.

Fish and aquatic invertebrates

For Complex soap 28 no acute toxic effects within the range of the water solubility were observed for fish and aquatic invertebrates. No long-term data were available for these two trophic levels.

Algae

Two studies were available investigating potential aquatic toxicity of Complex soap TH 28 to algae.

Complex soap TH 28 aquatic toxicity was assessed in an algae growth inhibition test (*Pseudokirchneriella subcapitata*) according to OECD Guideline 201 and EU Method C.3 (LAB Research Ltd (2010b)). As the test substance is slightly soluble in water and there is no GC- or HPLC method for quantification, a water accommodated fraction (WAF) of Complex soap TH 28

was prepared by dispersing the test item in a nominal load of 100 mg/L in test medium. The 72-h ErC50 was determined to be higher than 100 mg/L (WAF, equal to > 4.47 mg/L based on water solubility). Based on the WAF method applied no effects were noted at 50 mg/L (equivalent to 2.24 mg/L). Thus, a NOErC of 2.24 mg/L can be derived for this study.

The toxicity to algae (*Scenedesmus subspicatus*) was determined in a further study equivalent or similar to EU Method C.3 and OECD Guideline 201, resulting in 72-h ErC50 and NOErC values greater 1 mg/L (> 4.47 mg/L based on water solubility), equivalent to a concentration greater 100 mg/L (WAF) (ECHA (1991d)).

Overall, the results on Complex soap TH 28 obtained for aquatic toxicity testing reveal no potential danger to the environment in neither acute nor chronic tests even tested well above the water solubility. In all studies the EC50/LC50 and NOEC values were well above the water solubility (WAF) and also > 1 mg/L. Therefore, no classification and labelling for acute or chronic environmental hazard according to CLP Regulation is justified. The current classification for Aquatic Chronic 4 is most likely due for reasons of precaution as the log K_{ow} together with the limited information of water solubility and the limited biodegradation might indicate the potential for chronic toxic effects in the aquatic environment. The new data however support the conclusion that neither acute nor chronic effects on aquatic organisms are expected > 1 mg/L and in accordance with CLP Regulation no classification is triggered.

2.2.1 Current classification and labelling in Annex VI, Table 3.1 in the CLP Regulation

Classification

Skin Sens. 1, H317

Aquatic Chronic 4, H413

Labelling

GHS07, Warning (Wng)

H317, H413

2.3 Current self-classification and labelling

The industry self-classification(s) and labelling are publically available in the ECHA C&L Inventory¹.

¹ (<http://clp-inventory.echa.europa.eu/SummaryOfClassAndLabelling.aspx?SubstanceID=76448&HarmOnly=no?DisclaimerAgr=Agree&Index=58890-25-8&ExecuteSearch=true&fc=true&lang=en>)

3 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

For Complex soap TH 28 a harmonised classification had been developed under 67/548/EEC with the 29th ATP. Assessments performed in order to achieve registrations under REACH indicated that according to the re-evaluation of existing data and to evaluation of new data the existing classification for the toxicological class 'skin sensitization' and 'hazardous to the aquatic environment' no longer reflects the criteria for classification and labelling in Annex I of the CLP Regulation.

Based on the data available from former notifications and new study results generated, the registered substance Complex soap TH 28 is considered not dangerous to human health and not dangerous to the environment. Thus, classification and labelling as Skin Sensitiser 1; H317 as well as Aquatic Chronic 4 is not justified. Action is needed to revise the CLP Regulation entry in Annex VI table 3.1.

Part B.

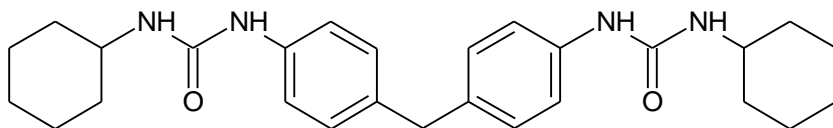
SCIENTIFIC EVALUATION OF THE DATA

1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 4: Substance identity

EC number:	406-370-3
EC name:	3,3'-dicyclohexyl-1,1'-methylenebis(4,1-phenylene)diurea
CAS number (EC inventory):	58890-25-8
CAS number:	58890-25-8
CAS name:	Urea, N,N''-(methylenedi-4,1-phenylene)bis[N'-cyclohexyl-
IUPAC name:	3,3'-dicyclohexyl-1,1'-methylenebis(4,1-phenylene)diurea
CLP Annex VI Index number:	616-094-00-7
Molecular formula:	C ₂₇ H ₃₆ N ₄ O ₂
Molecular weight range:	448.538 g/mol

Structural formula:**1.2 Composition of the substance****Table 5: Constituents (non-confidential information)**

Constituent	Typical concentration	Concentration range	Remarks
3,3'-dicyclohexyl-1,1'-methylenebis(4,1-phenylene)diurea		> 95 ≤ 100 % (w/w)	NA

Current Annex VI entry: H317, H413, (CLP)

For further information please see confidential annex or technical dossier.

Table 6: Impurities (non-confidential information)

Impurity	Typical concentration	Concentration range	Remarks

Current Annex VI entry: Not applicable.

Table 7: Additives (non-confidential information)

Additive	Function	Typical concentration	Concentration range	Remarks
No additives	--	--	--	--

Current Annex VI entry: Not applicable.

1.2.1 Composition of test material

The specifications for the test material are shown in the confidential annex or technical dossier.

1.3 Physico-chemical properties

Following table shows the relevant physical-chemical properties.

Table 8: Relevant physical-chemical properties

Property	Value	Reference	Comment (e.g. measured or estimated)
State of the substance at 20 °C and 101.3 kPa	solid	Klüber Lubrication München KG	TH28 is an organic odourless white solid.
Vapour pressure	111 Pa @ 25 °C (0.35 Pa @ 25 °C calculated for pure substance)	SNIF data	Robust study summary provided by ECHA
Water solubility	3.23 mg/L (DOC) equivalent to 4.47 mg/L test substance ^{*)}	LAB Research Ltd., 2010a	Determined according to OECD 105, EU method A.6
Partition coefficient n-octanol/water	log K _{OW} = 6.9	SNIF data	Robust study summary provided by ECHA

^{*)} The solubility of Complex soap TH 28 in water was determined using the shake flask method. As there is no GC- or HPLC-method available for the test item the dissolved organic carbon (DOC) content was determined resulting in 3.23 mg/L. As this represents the result obtained for the DOC part, the water solubility was recalculated for 3,3'-dicyclohexyl-1,1'-methylenebis(4,1-phenylene)diurea (Complex soap TH 28) as such, resulting in a water solubility based on the carbon content of 72.3% of 4.47 mg/L. It should however be noted, that the method used is not substance specific (DOC) which analyses the substance as such as well as potential impurities. Thus the real water solubility might slightly be lower as the values obtained.

2 MANUFACTURE AND USES

2.1 Manufacture

Confidential information.

2.2 Identified uses

Lubrication or lubrication additive.

3 CLASSIFICATION FOR PHYSICO-CHEMICAL PROPERTIES

Based on results obtained classification and labelling for physical-chemical properties according to CLP Regulation is not justified.

4 HUMAN HEALTH HAZARD ASSESSMENT

The following section shows relevant data on human health hazard assessment.

4.1 Toxicokinetics (absorption, metabolism, distribution and elimination)

Hazard class not evaluated in this dossier.

4.2 Acute toxicity

Hazard class not evaluated in this dossier.

4.3 Irritation

Hazard class not evaluated in this dossier.

4.4 Corrosivity

Hazard class not evaluated in this dossier.

4.5 Sensitisation

4.5.1 Skin sensitisation

4.5.1.1 Non-human information

The results of experimental studies on skin sensitisation are summarised in the following table:

Table 9: Summary table of relevant skin sensitisation studies

Method	Results	Remarks	Reference
mouse (CBA/J) female Local lymph node assay (LLNA) OECD Guideline 429 (Skin Sensitisation: Local Lymph Node Assay) (1998) EU Method B.42 (Skin Sensitisation: Local Lymph Node Assay) (2008)	not sensitising Stimulation index (SI): The lack of any positive result under these exaggerated test conditions is considered to be good evidence that Complex soap TH 28 is not a sensitizer. The stimulation index values were 0.5, 0.5 and 0.7 at concentrations of 10 %, 5 % and 2.5 %, respectively, which were negative due to SI < 3 . Positive control: 25 % α Hexylcinnamaldehyde (HCA, CAS 101-86-0): SI = 4.9 (positive, SI \geq 3)	1 (reliable without restriction) key study experimental result Test material (EC name): 3,3'-dicyclohexyl-1,1'-methylenebis(4,1-phenylene)diurea	Török-Bathó, M (2009)

Mouse Local Lymph Node Assay

The skin sensitisation potential of Complex soap TH 28 (Lot/batch No. AH-1290/2009-02, analytical purity > 95 %) was tested in a Local Lymph Node Assay (LLNA) performed in CBA/J@Rj mice according to OECD Guideline 429 and EU Method B.42.

Prior to the main study, vehicle compatibility of Complex soap TH 28 was verified in a preliminary compatibility test with acetone:olive oil 4:1 (v/v) mixture (AOO), *N,N*-Dimethylformamide, Ethyl-methylketone, Dimethyl sulfoxide, Propylene-glycol and *n*-Hexane:olive oil 4:1 (v/v) mixture (HOO). The most suitable vehicle was found to be AOO, with a maximum available test item concentration of 10 % (w/v). The test item was insoluble in all other solvents. Further, a preliminary irritation/toxicity test was performed with Complex soap TH 28 in CBA/J@Rj mice at concentrations of 10 % and 5 % in AOO. The applicability and biocompatibility of Complex soap TH 28 on ears of animals was found to be acceptable up to the maximum available concentration of 10 %.

In the main study sixteen female CBA/J@Rj mice were randomly assigned to four groups. Three groups were treated with Complex soap TH 28 at concentrations of 10 %, 5 % and 2.5 %. The control group was treated with the vehicle AOO. The test item solutions were applied on the dorsal surface of ears of the animals (25 µL/ear) for three consecutive days (days 1, 2 and 3). After application of the 10 % and 5 % test item solutions on ears of animals, a precipitate on the treatment area was observed. There was no treatment on days 4, 5 and 6. On day 6, the cell proliferation in local lymph nodes was determined by measuring the incorporation of tritiated methyl thymidine (³HTdR). The values obtained from analysis were used to calculate stimulation indices (SI). No mortality, no local toxicity or systemic clinical signs were observed during the study. No treatment related effect on body weight was observed. Additionally, no irritation or other local effects were observed. SI values of the test item were 0.5, 0.5 and 0.7 at treatment concentrations of 10 %, 5 % and 2.5 %, respectively.

The results of the latest reliability check (performed within an interval of no longer than six months), was used to demonstrate the appropriate performance of the assay in accordance with the OECD Guideline 429. The positive control substance α -Hexylcinnamaldehyde (HCA, CAS 101-86-0) was examined at a concentration of 25 % in the vehicle AOO. A significant proliferation of lymphocytes in the lymph nodes draining the site of the test substance application was noted for the positive control substance HCA with a SI value of 4.9, which is positive due to $SI \geq 3$ and confirms the validity of the LLNA in the performing laboratory. The following table gives an overview of test results from the LLNA with Complex soap TH 28 and the positive control substance HCA performed in female CBA/J@Rj mice.

Table 10: Results of the LLNA with complex soap TH 28 performed in female CBA/J@Rj mice

Test concentration	Stimulation Index (SI)	Result
10 % Complex soap TH 28	0.5	Negative (SI < 3)
5 % Complex soap TH 28	0.5	Negative (SI < 3)
2.5 % Complex soap TH 28	0.7	Negative SI < 3)
25 % HCA, positive control substance	4.9	Positive (SI \geq 3)

Thus, no SI value of 3 or more was noted for all three tested concentrations of Complex soap TH 28 and further, there was no dose-related response, which indicates a negative result in this test system.

In conclusion, no skin sensitizing properties were observed in female CBA/J@Rj mice after treatment with Complex soap TH 28 at concentrations of 10 %, 5 % and 2.5 %.

4.5.1.2 Human information

No data available.

4.5.1.3 Summary and discussion of skin sensitisation

In a guideline-compliant mouse LLNA no skin sensitizing properties of Complex soap TH 28 was found. The skin sensitisation potential of Complex soap TH 28 was tested in a LLNA performed in CBA/J@Rj mice according to OECD Guideline 429 and EU Method B.42. SI values of the test item were 0.5, 0.5 and 0.7 at treatment concentrations of 10 %, 5 % and 2.5 %, respectively. Thus, the ratio of the mean proliferation in each treated test group to that in the concurrent control group was lower than the cut-off value of 3. Further, there was no dose-related response. The results have shown that Complex soap TH 28 does not point to a skin sensitizing potential in mice after dermal application.

4.5.1.4 Comparison with criteria

(i) Identification of hazard information: *'Skin sensitiser means a substance that will lead to an allergic response following skin contact.'*

There is no information available with respect to skin sensitisation of Complex soap TH 28 from case reports, epidemiological studies, medical surveillance and reporting schemes based on human patch testing. Data for skin sensitisation of Complex soap TH 28 was obtained from animal testing according to existing testing guidelines.

(ii) Classification criteria for substances, Hazard categories: *'substances shall be classified as skin sensitisers (Category 1) where data are not sufficient for sub-categorisation in accordance with the following criteria: (a) if there is evidence in humans that the substance can lead to sensitisation by skin contact in a substantial number of persons; or (b) if there are positive results from an appropriate animal test. For Category 1, a stimulation index (SI) of three or more is considered a positive response in the local lymph node assay.'*

The skin sensitisation potential (hazard identification) of Complex soap TH 28 was tested in a murine LLNA according to OECD Guideline 429 and EU Method B.42. SI values of the test item were 0.5, 0.5 and 0.7 at treatment concentrations of 10 %, 5 % and 2.5 %, respectively. None of the three tested concentrations of Complex soap TH 28 have shown a SI value of 3 or more. Furthermore, there was no dose-related response. In conclusion, in a guideline-compliant murine LLNA, Complex soap TH 28 did not induce skin sensitisation in mice.

(iii) Sub-categories for skin sensitisers: *'Skin sensitiser shall be classified in Category 1 where data are not sufficient for sub-categorisation (CLP Annex I 3.4.2.2.1.1).'*

Potential for skin sensitisation (hazard identification) was not determined for Complex soap TH 28. Accordingly, relative skin sensitisation potency (hazard characterisation) was not calculated.

4.5.1.5 Conclusions on classification and labelling

Based on the negative results obtained from a LLNA in mice classification and labelling of Complex soap TH 28 for skin sensitisation is not justified according to the CLP Regulation. Therefore removal of the classification of the registered substance Complex soap TH 28 as Skin Sens.1 (H317) is proposed.

4.5.2 Respiratory sensitisation

Data lacking. Hazard class not assessed in this dossier.

4.6 Repeated dose toxicity

Hazard class not evaluated in this dossier.

4.7 Specific target organ toxicity (CLP Regulation) – repeated exposure (STOT RE)

Not applicable.

4.8 Germ cell mutagenicity (Mutagenicity)

Hazard class not evaluated in this dossier.

4.9 Carcinogenicity

Hazard class not evaluated in this dossier.

4.10 Toxicity for reproduction

Hazard class not evaluated in this dossier.

4.11 Other effects

Hazard class not evaluated in this dossier.

5 ENVIRONMENTAL HAZARD ASSESSMENT

5.1 Degradation

The test results are summarised in the following table:

Table 11: Summary table of results from relevant degradation studies

Method	Results	Remarks	Reference
equivalent or similar to OECD Guideline 301 A (old version) (Ready Biodegradability: Modified AFNOR Test)	Not readily biodegradable % Degradation of test substance: 48 after 28 d	3 (not reliable) key study experimental result Test material (EC name): 3,3'-dicyclohexyl-1,1'-methylenebis(4,1-phenylene)diurea	ECHA (1991e)

Discussion

A guideline study performed according to OECD 301 A reached a value of 48 % degradation within 28 days. However, the OECD 301 A is not suitable for poorly soluble (< 100mg/L) compounds. No other degradation data are available. Therefore, Complex soap TH28 should be regarded by default as not rapidly degradable (ECHA Guidance on the Application of the CLP Criteria Annex II.2.4).

5.2 Environmental distribution

5.3 Aquatic Bioaccumulation

The high log K_{ow} of 6.9 indicates potential for bioaccumulation. Estimates for the Soil Adsorption Coefficient (log K_{oc}) and Henry's law constant were made using EPIWIN (v.4.11). The values obtained are 3.968 for the log K_{oc} (K_{ow} method, KOCWIN v2.00) and $6.74 \cdot 10^{-21}$ atm·m³·mol⁻¹ for the Henry's law constant at 25 °C (Bond method, HENRYWIN v3.20) (see Annex).

5.4 Aquatic toxicity

5.4.1 Fish

5.4.1.1 Short-term toxicity to fish

Table 12: Summary of relevant information on potential aquatic toxicity to fish

Method	Results	Remarks	Reference
<i>Brachydanio rerio</i> (new name: <i>Danio rerio</i>) Equivalent or similar to OECD Guideline 203 (Fish, Acute Toxicity Test) EU Method C.1 (Acute toxicity for fish) Limit test	LC50 (96 h): > 100 mg/L (nominal), respectively > maximal water solubility (> 4.47 mg/L based on water solubility),	2 (reliable with restriction – no analytical monitoring) key study experimental result Test material (EC name): 3,3'-dicyclohexyl-1,1'-methylenebis(4,1-phenylene)diurea	ECHA (1991b)

Discussion

Complex soap TH 28 acute toxicity to fish was determined in a study equivalent or similar to EU Method C.1 and OECD Guideline 203. Exposure to freshwater fish *Brachydanio rerio* (new name: *Danio rerio*) was investigated, resulting in a 96-hour LC50 value greater 100 mg/L (> 4.47 mg/L based on water solubility)). No effects were noted at all even tested well above the water solubility.

The test substance is slightly soluble in water and there is no GC or HPLC method for quantification. Based on the information available, most likely a limit test was carried out using direct addition of the test substance to the test medium.

5.4.1.2 Long-term toxicity to fish

No data available.

5.4.2 Aquatic invertebrates

5.4.2.1 Short-term toxicity to aquatic invertebrates

Table 13: Summary of relevant information on potential aquatic toxicity to invertebrates

Method	Results	Remarks	Reference
<i>Daphnia magna</i> Equivalent or similar to OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test) EU Method C.2 (Acute toxicity for Daphnia) Limit test	EC50 (48 h): > 100 mg/L (nominal) (> 4.47 mg/L based on water solubility)	2 (reliable with restriction – no analytical monitoring) key study experimental result Test material (EC name): 3,3'-dicyclohexyl-1,1'-methylenebis(4,1-phenylene)diurea	ECHA (1991c)

Discussion

Complex soap TH 28 acute toxicity to invertebrates was determined in a study equivalent or similar to EU Method C.2 and OECD Guideline 202. Exposure to *Daphnia* was investigated, resulting in a 48-hour EC50 value greater 100 mg/L (> 4.47 mg/L based on water solubility). No effects were noted at all even tested well above the water solubility.

The test substance is slightly soluble in water and there is no GC or HPLC method for quantification. Most likely a limit test was carried out using direct addition of the test substance to the test medium.

5.4.2.2 Long-term toxicity to aquatic invertebrates

No data available.

5.4.3 Algae

Table 14: Summary of relevant information on potential aquatic toxicity to algae

Method	Results	Remarks	Reference
<i>Pseudokirchnerella subcapitata</i> (algae) freshwater static EU Method C.3 (Algal Inhibition test) OECD Guideline 201 (Alga, Growth Inhibition Test)	EC50 (72 h): > 100 mg/L test mat. (nominal); > 4.47 mg/L based on water solubility/ nominal) based on: growth rate NOEC (72 h): 50 mg/L test mat. (nominal); 2.24 mg/L based on water solubility/ nominal) based on: growth rate LOEC (72 h): 100 mg/L test mat. (nominal); 4.47 mg/L based on water solubility/ nominal) based on: growth rate	2 (reliable with restriction – no analytical monitoring) key study experimental result Test material (EC name): 3,3'-dicyclohexyl-1,1'-methylenebis(4,1-phenylene)diurea	LAB Research Ltd. (2010b)
<i>Scenedesmus subspicatus</i> (new name: <i>Desmodesmus subspicatus</i>) (algae) Equivalent or similar to EU Method C.3 (Algal Inhibition test) OECD Guideline 201 (Alga, Growth Inhibition Test) Limit test	EC50 (72 h): > 100 mg/L (nominal) (> 4.47 mg/L based on water solubility) (based on: biomass EC50 (72 h): > 100 mg/L (nominal) (> 4.47 mg/L based on water solubility) based on: growth rate NOEC (72 h): > 100 mg/L (nominal) (> 4.47 mg/L based on water solubility) based on: growth rate NOEC (72 h): > 100 mg/L (nominal) (> 4.47 mg/L based on water solubility) based on: biomass	2 (reliable with restriction – no analytical monitoring) supporting study experimental result Test material (EC name): 3,3'-dicyclohexyl-1,1'-methylenebis(4,1-phenylene)diurea	ECHA (1991d)

Discussion

Algae

Two studies were available investigating potential aquatic toxicity of Complex soap TH 28 to algae.

Key study

Complex soap TH 28 aquatic toxicity was assessed in an algae growth inhibition test according to OECD Guideline 201 and EU Method C.3 (LAB Research Ltd (2010b)). As the test substance is slightly soluble in water (water solubility = 4.47 mg/L) and there is no GC or HPLC method for quantification, according to the registrant a water accommodated fraction (WAF) of Complex soap TH 28 was prepared by dispersing the test item in a nominal load of 100 mg/L in test medium. The solution was vigorously shaken for 24 h at approximately 30 °C. Subsequently, the solution was left

settling for 24 hours at approximately 20 °C and thereafter filtrated through a 0.22 µm pore filter. The corresponding nominal test item concentrations were: 6.25; 12.5; 25.0; 50.0 and 100.0 mg/L. The OECD “Guidance document on aquatic toxicity testing of difficult substances and mixtures” No. 23 describes at page 36 that “WAFs are prepared individually and not by serial dilution of a single stock WAF.” Therefore the method used in the key algae study is no true WAF-method. Here, only the highest test concentration was prepared individually. As stated above, no GC or HPLC method for quantification exists. Therefore nominal concentrations had to be used for the assessment of Complex soap TH28.

Exponentially growing cultures of *Pseudokirchneriella subcapitata* were exposed for up to 72 h. The algae growth in relation to a control culture was determined. Based on the results the 72-h EC50 value for growth rate (ErC) and the NOEC value for growth rate (NOErC) were clearly above 1 mg/L. Based on the WAF method applied no effects (NOEC) were noted at 50 mg/L (nominal) (equivalent to 2.24 mg/L). The LOEC is 4.47 mg/L (at water solubility).

Supporting study

Complex soap TH 28 acute toxicity to algae was also determined in a study equivalent or similar to EU Method C.3 and OECD Guideline 201 (ECHA (1991d)). Exposure to exponentially growing cultures of *Scenedesmus subspicatus* was investigated, resulting in a 72-hour EC50 value (growth rate, ErC) greater 100 mg/L (nominal) (> 4.47 mg/L based on water solubility).

No effects were noted at all even tested well above the water solubility.

The test substance is slightly soluble in water and there is no GC or HPLC method for quantification. Most likely a limit test was carried out using a direct addition of the test substance to the test medium.

5.4.4 Other aquatic organisms (including sediment)

No data available.

5.5 Comparison with criteria for environmental hazards (sections 5.1 – 5.4)

Table 15: Comparison with criteria for environmental hazards (sections 5.1-5.6)

	Criteria for environmental hazards		Complex soap TH28	Conclusion
	CLP			
Rapid Degradation	Readily biodegradable in a 28-day test for ready biodegradability		no useful data available	not rapidly degradable
Bioaccumulation	BCF ≥ 500 Log K _{ow} ≥ 4		Log Kow = 6.9	bioaccumulative
Aquatic Toxicity	NOEC ≤ 1 mg/L	LC50/EC50 ≤ 100 mg/L	Fish: LC50 (96 h) > water solubility; No chronic data available Invertebrates: EC50 (48 h) > water solubility; No chronic data available Algae: ErC50 (72 h) > water solubility; chronic data available: NOErC (72 h) > 1 mg/L	LC50/EC50 > water solubility; and there is scientific evidence showing classification is unnecessary with a chronic toxicity NOEC > 1 mg/L

5.6 Conclusions on classification and labelling for environmental hazards (sections 5.1 – 5.4)

Complex soap TH 28 is not rapidly degradable and bioaccumulative. Nevertheless, the entire data set revealed no acute toxic effects in the range of the water solubility and no chronic toxic effects below 1 mg/L. Hence, Complex soap TH 28 does not fulfil the criteria for environmental hazards according to CLP-Regulation. As there is scientific evidence showing classification is unnecessary with a chronic toxicity NOEC > 1 mg/L from the algae test, the existing classification, Aquatic Chronic 4, should be removed.

6 OTHER INFORMATION

Not applicable.

7 REFERENCES

CLP Regulation No. 1272/2008 on classification, labelling and packaging of substances and mixtures; (2008).

ECHA (1991a). Testing laboratory: no data. Report no.: SNIF#001-3.0.40-01

ECHA (1991b). Testing laboratory: no data. Report no.: SNIF#001-5.1.01-01.

ECHA (1991c). Testing laboratory: no data. Report no.: SNIF#001-5.1.02-01.

ECHA (1991d). Testing laboratory: RCC, Research and consulting company AG, 4452 Itingen. Report no.: SNIF#001-5.1.03-01.

ECHA (1991e). Testing laboratory: no data. Report no.: SNIF#001-5.2.11-01.

LAB Research Ltd.; (2010a). Water Solubility Determination of Complex soap TH 28. Testing laboratory: LAB Research Ltd.; 8200 Veszprém, Szabadságpuszta; Hungary. Report no.: 09/057-345AN. Owner company: Klüber Lubrication München KG; Geisenhausenerstr. 7; D-81379 Munich; Germany. Report date: 2010-12-10.

LAB Research Ltd.; (2010b). Growth Inhibition Test of Complex soap TH 28 on Algae (*Pseudokirchneriella subcapitata*). Testing laboratory: LAB Research Ltd.; 8200 Veszprém, Szabadságpuszta; Hungary. Report no.: 10/236-022AL. Owner company: Klüber Lubrication München KG; Geisenhausenerstr. 7; D-81379 Munich; Germany. Report date: 2010-12-10.

REACH Regulation No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorization and Restriction of Chemicals; (2006)

Török-Bathó, M (2009); LAB Research Ltd.; Skin Sensitisation: Local Lymph Node Assay with Complex soap TH 28. Testing laboratory: LAB Research Ltd. H-8200 Veszprém, Szabadságpuszta, Hungary. Report no.: 09/057-037E. Owner company: Klüber Lubrication München KG, Geisenhausenerstr. 7, D-81379 Munich, Germany. Report date: 2010-01-07.

8 ANNEXES

Summary EPIWIN (v.4.11).