Danish Ministry of the Environment
Environmental Protection Agency

Justification Document for the Selection of a CoRAP Substance

Substance Name (public name):	**Formaldehyde, oligomeric reaction products with 1-chloro-2,3-epoxypropane and phenol**
EC Number:	**500-006-8**
CAS Number:	**9003-36-5**
Authority:	**DK MSCA**
Date:	**22/03/2016**

Note

This document has been prepared by the evaluating Member State given in the CoRAP update.

Contents

1 IDENTITY OF THE SUBSTANCE

1.1 Other identifiers of the substance

Table: Other Substance identifiers

EC name (public):	500-006-8
IUPAC name (public):	Formaldehyde, oligomeric reaction products with 1-chloro-2,3-epoxypropane and phenol
Index number in Annex VI of the CLP Regulation:	-
Molecular formula:	Multi constituent substance
Molecular weight or molecular weight range:	<= 700.0
Synonyms:	*Araldite® GY 281;* *Araldite® GY 282;* *Araldite® GY 783;* *Araldite® PY 307-1;*

Type of substance ☐ Mono-constituent ☒ Multi-constituent ☐ UVCB

Structural formula:

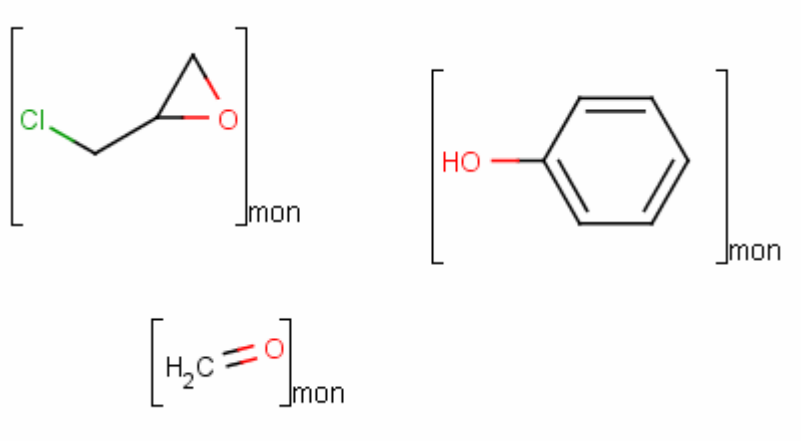
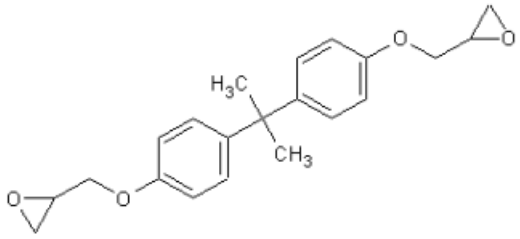
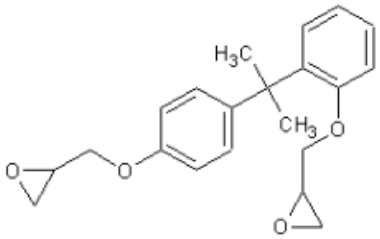
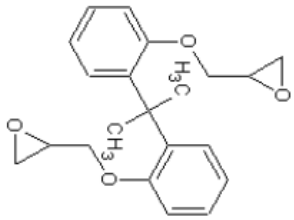
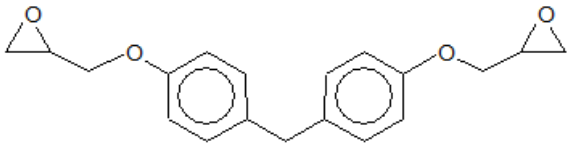
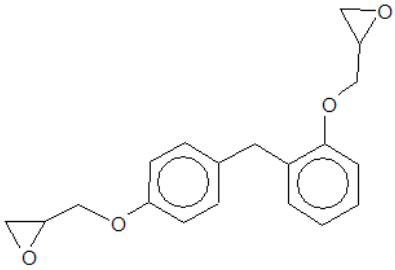
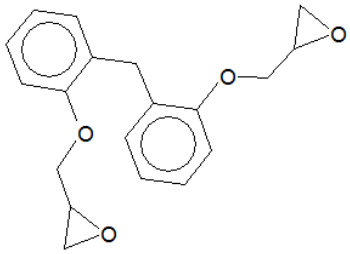
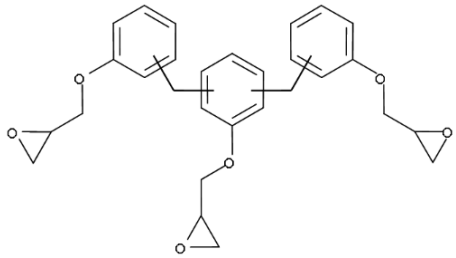
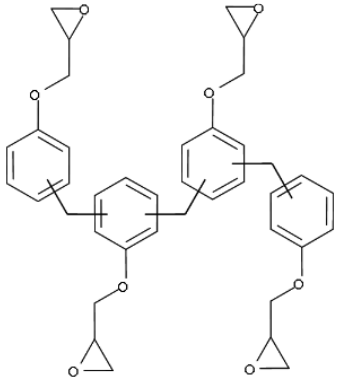
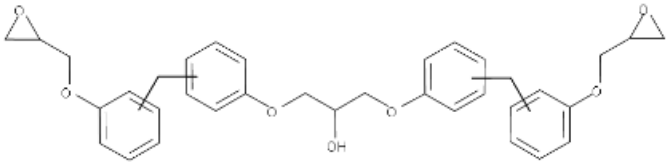
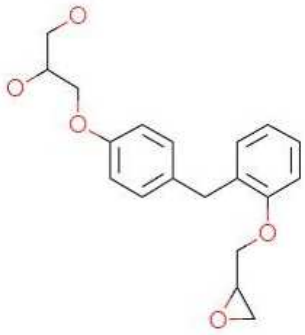
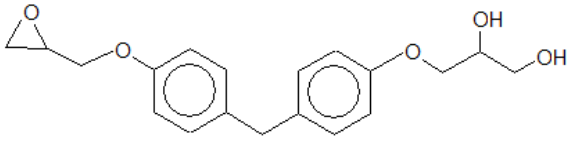
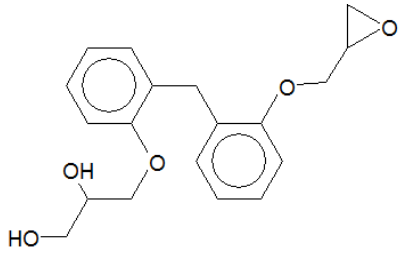


Table: Constituent

Name, CAS number, SMILES	Structural formula
2,2'-[propane-2,2-diylbis(benzene-4,1-diyloxymethanediyl)]dioxirane CAS RN: 1675-54-3 SMILES: CC(C)(c2ccc(OCC1CO1)cc2)c4ccc(OCC3CO3)cc4	
2-[(2-{2-[4-(oxiran-2-ylmethoxy) phenyl]propan-2-yl}phenoxy) methyl]oxirane CAS RN: N.A. SMILES: CC(C)(c2ccccc2OCC1CO1)c4ccc(OCC3CO3)cc4	
2,2'-[propane-2,2-diylbis(benzene-2,1-diyloxymethanediyl)]dioxirane CAS RN: N.A. SMILES: CC(C)(c2ccccc2OCC1CO1)c4ccccc4OCC3CO3	
2,2'-[methylenebis(p-phenyleneoxy methylene)]bisoxirane CAS RN: 2095-03-6 SMILES: C(C1CO1)Oc1ccc(Cc2ccc(OCC3CO3)cc2)cc1	
[[2-[p-(oxiranylmethoxy)benzyl] phenoxy]methyl]oxirane CAS RN: 57469-07-5 SMILES: C(C1CO1)Oc1ccccc1Cc1ccc(OCC2CO2)cc1	
2,2'-[methylenebis(o-phenyleneoxy methylene)]bisoxirane CAS RN: 54208-63-8 SMILES: C(C1CO1)Oc1ccccc1Cc1ccccc1OCC1CO1	

2,2′,2″-[dimethylenetri(phenyleneoxy methylene)]trioxirane CAS RN: N.A. SMILES: N.A.	
2,2′,2″,2‴-[trimethylenetetra (phenyleneoxymethylene)]tetraoxirane CAS RN: N.A. SMILES: N.A.	
2-Propanol, 1,3-bis[2,2′-[methylenedi (phenyleneoxymethylene)]bisoxirane] CAS RN: N.A. SMILES: N.A.	
1,2-Propanediol, 3-[2-[[4-(2-oxiranylmethoxy)phenyl]methyl]phenoxy] CAS RN: N.A. SMILES: N.A.	
3-[4-[[4-(2-oxiranylmethoxy)phenyl] methyl]phenoxy]-1,2-propanediol CAS RN: N.A. SMILES: OCC(O)COc3ccc(Cc2ccc(OCC1CO1)cc2)cc3	
1,2-Propanediol, 3-[2-[[2-(2-oxiranyl methoxy)phenyl]methyl]phenoxy] CAS RN: N.A. SMILES: OCC(O)COc1ccccc1Cc2ccccc2OCC3CO3	

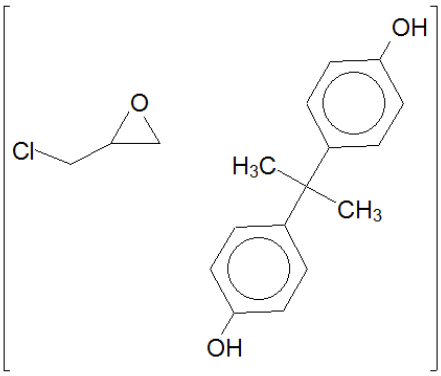
1.2 Similar substances/grouping possibilities

The substance is structurally similar to BPA Epoxy Resin which is nominated for the CoRAP list and under substance evaluation in 2015 with DK as the evaluating MSCA.

Table: Similar substance

EC number:	500-033-5
EC name (public):	4,4'-Isopropylidenediphenol, oligomeric reaction products with 1-chloro-2,3-epoxypropane
CAS number:	25068-38-6
CAS name (public):	-
IUPAC name (public):	
Index number in Annex VI of the CLP Regulation:	603-074-00-8
Molecular formula:	N.A.
Molecular weight or molecular weight range:	≥ 340 - ≤ 700
Synonyms:	Bisphenol A, epichlorhydrin epoxy resin Average MW < 700. 2-(chloromethyl)oxirane; 4-[2-(4-hydroxyphenyl)propan-2-yl]phenol; 4,4'-Isopropylidenediphenol, oligomeric reaction products with 1-chloro-2,3-epoxypropane; Bisphenol A epoxy resin;

Structural formula:



2 OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Table: Completed or ongoing processes

RMOA	☐ Risk Management Option Analysis (RMOA)	
REACH Processes	Evaluation	☒ Compliance check, Final decision The compliance check decision was issued by ECHA in 2012 and contained requests for substance ID related information.
		☐ Testing proposal
		☐ CoRAP and Substance Evaluation
	Authorisation	☐ Candidate List
		☐ Annex XIV
	Restri -ction	☐ Annex XVII
Harmonised C&L	☐ Annex VI (CLP) (see section 3.1)	
Processes under other EU legislation	☐ Plant Protection Products Regulation Regulation (EC) No 1107/2009	
	☐ Biocidal Product Regulation Regulation (EU) 528/2012 and amendments	
Previous legislation	☐ Dangerous substances Directive Directive 67/548/EEC (NONS)	
	☐ Existing Substances Regulation Regulation 793/93/EEC (RAR/RRS)	
Stockh olm convent ion (POPs Protoco	☐ Assessment	

	☐ In relevant Annex
Other processes/ EU legislation	☒ Other (provide further details below) Evaluated by EFSA for genotoxicity in 2005 (http://www.efsa.europa.eu/de/scdocs/doc/274.pdf)

3 HAZARD INFORMATION (INCLUDING CLASSIFICATION)

3.1 Classification

3.1.1 Harmonised Classification in Annex VI of the CLP

No harmonised classification

3.1.2 Self classification

- In the registration:
    - Skin Irrit. 2 H315: Causes skin irritation.
    - Skin Sens. 1 H317: May cause an allergic skin reaction.
    - Aquatic Chronic 2 H411: Toxic to aquatic life with long lasting effects.

- The following hazard classes are in addition notified among the aggregated self classifications in the C&L Inventory:
    - Acute Tox. 3 H311
    - Eye Irrit. 2 H319
    - Aquatic Chronic 4 H413
    - Not classified

3.1.3 Proposal for Harmonised Classification in Annex VI of the CLP

Not available

4 INFORMATION ON (AGGREGATED) TONNAGE AND USES

4.1 Tonnage and registration status

Table: Tonnage and registration status

From ECHA dissemination site		
☒ Full registration(s) (Art. 10)	☐ Intermediate registration(s) (Art. 17 and/or 18)	
Tonnage band (as per dissemination site)		
☐ 1 – 10 tpa	☐ 10 – 100 tpa	☐ 100 – 1000 tpa
☐ 1000 – 10,000 tpa	☒ 10,000 – 100,000 tpa	☐ 100,000 – 1,000,000 tpa
☐ 1,000,000 – 10,000,000 tpa	☐ 10,000,000 – 100,000,000 tpa	☐ > 100,000,000 tpa
☐ <1 . . . . . >+ tpa (e.g. 10+ ; 100+ ; 10,000+ tpa)		☐ Confidential

4.2 Overview of uses

Formaldehyde, oligomeric reaction products with 1-chloro-2,3-epoxypropane and phenol is used in coatings, in paints and adhesives, as monomers in the production of epoxy-based polymers and as additives.

Table: Uses

☒ Manufacture	☒ Formulation	☒ Industrial use	☒ Professional use	☒ Consumer use	☒ Article service life	☒ Closed system

5. JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

5.1. Legal basis for the proposal

☒ Article 44(2) (refined prioritisation criteria for substance evaluation)

☐ Article 45(5) (Member State priority)

5.2. Selection criteria met (why the substance qualifies for being in CoRAP)

☐ Fulfils criteria as CMR/ Suspected CMR

☐ Fulfils criteria as Sensitiser/ Suspected sensitiser

☒ Fulfils criteria as potential endocrine disrupter

☐ Fulfils criteria as PBT/vPvB / Suspected PBT/vPvB

☒ Fulfils criteria high (aggregated) tonnage (*tpa > 1000*)

☒ Fulfils exposure criteria

☐ Fulfils MS's (national) priorities

5.3 Initial grounds for concern to be clarified under Substance Evaluation

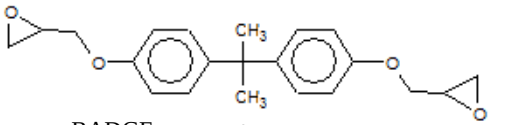
Hazard based concerns		
CMR ☐ C ☐ M ☐ R	Suspected CMR[1] ☐ C ☐ M ☐ R	☒ Potential endocrine disruptor
☐ Sensitiser	☐ Suspected Sensitiser[1]	
☐ PBT/vPvB	☐ Suspected PBT/vPvB[1]	☐ Other (please specify below)

Exposure/risk based concerns		
☐ Wide dispersive use	☐ Consumer use	☐ Exposure of sensitive populations
☐ Exposure of environment	☐ Exposure of workers	☐ Cumulative exposure
☐ High RCR	☐ High (aggregated) tonnage	☐ Other (please specify below)

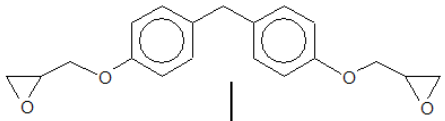
Very limited *in vivo* information is available for endocrine related endpoints for the registered substance. In the registration dossier, read across is performed to the structurally similar substance BADGE (CAS 1675-54-3) to fill the standard information data gap on a two-generation reproductive toxicity study (OECD TG 416). In the robust study summary reported by the registrants there are no recordings of effects in this study which would raise a concern for endocrine disruption. The validity of the proposed read across has not been yet evaluated.

A few *in vitro* studies on endocrine related endpoints are recorded from peer reviewed articles for BADGE and BFDGE which are constituents in the registered substance. According to Satoh *et al*. (2004) and Nakazawa *et al.* (2002) no estrogenic activity were identified when testing the parent compounds. However, both substances were found to have binding affinity to the androgen receptor and to display weak AR antagonist activity.

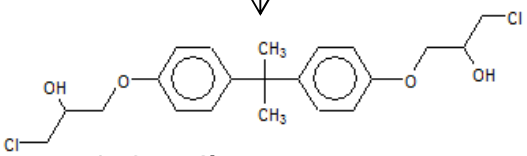
One of the uses of the registered substance is to remove surplus hydrochloric acid in PVC production. The resulting chlorinated transformation products of BADGE and BFDGE have also been tested *in vitro.*



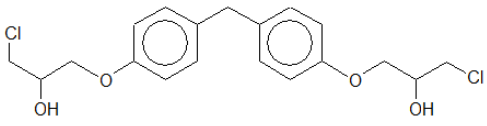
BADGE



BFDGE



BADGE.2HCl



BFDGE.2HCl

Nakazawa *et al.* (2002) examined the estrogenic activity of BADGE.2HCl and BADGE.4OH (another BADGE transformation product) in the estrogen receptor (ER) alpha binding assay and in the breast cancer cell (T47D) profileration assay. Both transformation products

[1] CMR/Sensitiser: known carcinogenic and/or mutagenic and/or reprotoxic properties/known sensitising properties (according to CLP harmonized or registrant self-classification or CLP Inventory)
Suspected CMR/Suspected sensitiser: suspected carcinogenic and/or mutagenic and/or reprotoxic properties/suspected sensitising properties (not classified according to CLP harmonized or registrant self-classification)
Suspected PBT: Potentially Persistent, Bioaccumulative and Toxic

displayed estrogenic activity in the cell profileration assay but did not bind to the estrogen receptor. Based on this the authors indicate that these transformation products can display estrogenic activity through another mechanism than ER binding.

Satoh *et al*. (2004) did not identify estrogenic activity of BADGE.2HCl and BFDGE.2HCL in an estrogen receptor reporter gene assay. However, in an androgen receptor luciferase assay both transformation products displayed a high binding affinity for the androgen receptor and also strong AR antagonistic activity.

Based on the above cited *in vitro* studies on the transformation products of BADGE and BFDGE and on the lack of relevant *in vivo* data for endocrine related endpoints a concern is raised which should be investigated further. Therefore, the substance "Formaldehyde, oligomeric reaction products with 1-chloro-2,3-epoxypropane and phenol" has been nominated for the CORAP list with the purpose to clarify if the indicated concern for endocrine disrupting properties is realized or not.

References

Nakazawa, H., Yamaguchi, A., Inoue,K., Yamazaki, T., Kato, K., Yoshimura, Y., Makino, T. 2002. In vitro assay of hydrolysis and chlorohydroxy derivatives of bisphenol A diglycidyl ether for estrogenic activity. Food and Chemical Toxicology 40: 1827-1832.

Satoh, K., Ohyama, K., Aoki, N., Lida, M., Nagai, F. 2004. Study on anti-androgenic effects of bisphenol a diglycidyl ether (BADGE), bisphenol F diglycidyl ether (BFDGE) and their derivatives using cells stably transfected with human androgen receptor, AR-EcoScreen. Food and Chemical Toxicology 42: 983-993.

5.4 Preliminary indication of information that may need to be requested t clarify the concern

☒ Information on toxicological properties	☐ Information on physico-chemical properties
☒ Information on fate and behaviour	☐ Information on exposure
☐ Information on ecotoxicological properties	☒ Information on uses
☒ Information ED potential	☐ Other (provide further details below)

Different approaches may be considered in order to clarify the identified concern. Depending on the outcome of a more thorough evaluation it may be considered relevant to request test data to clarify the hazard profile (with a focus on ED properties) of the registered substance and/or its transformation products. Alternatively, it could be considered to first clarify the relevance of the transformation products in hazard or risk assessment of the registered substance (i.e. the degree of formation during the life cycle of the substance).

5.5 Potential follow-up and link to risk management

☐ Harmonised C&L	☐ Restriction	☒ Authorisation	☐ Other (provide further details)

If the substance is an endocrine disrupter a SVHC proposal should be considered.