Danish Ministry of the Environment
Environmental Protection Agency

Justification Document for the Selection of a CoRAP Substance

- Update -

Substance Name (public name):	Reaction mass of 2,2'-[methylenebis(2,1-phenyleneoxymethylene)]bis(oxirane) and 2,2'-[methylenebis(4,1-phenyleneoxymethylene)]bis(oxirane) and 2-({2-[4-(oxiran-2-ylmethoxy)benzyl]phenoxy}methyl)oxirane)
EC Number:	701-263-0
CAS Number:	n/a
Authority:	Danish Environmental ProtectionAgency
Date:	22/03/2016 18/03/2020 (1. update)

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):	2-(2-{[2-(oxiran-2-ylmethoxy)phenyl]methyl}phenoxymethyl)oxirane; 2-(2-{[4-(oxiran-2-ylmethoxy)phenyl]methyl}phenoxymethyl)oxirane; 2-(4-{[4-(oxiran-2-ylmethoxy)phenyl]methyl}phenoxymethyl)oxirane
EC and CAS number	EC 701-263-0 , no CAS no (previously EC 500-006-8, CAS no 9003-36-5)
IUPAC name (public):	Formaldehyde, oligomeric reaction products with 1-chloro-2,3-epoxypropane and phenol
Other IUPAC names	Formaldehyde, oligomeric reaction products with 1-chloro-2,3-epoxypropane and phenol/BPFDGE Reaction mass of 2,2'-[methylenebis(2,1-phenyleneoxymethylene)]bis(oxirane) and 2,2'-[methylenebis(4,1-phenyleneoxymethylene)]bis(oxirane) and 2-({2-[4-(oxiran-2-ylmethoxy)benzyl]phenoxy}methyl)oxirane Reaction mass of 2,2'-[methylenebis(4,1-phenyleneoxymethylene)]dioxirane and [2-({2-[4-(oxiran-2-ylmethoxy)benzyl]phenoxy}methyl)oxirane and [2,2'-[methylenebis(2,1-phenyleneoxymethylene)]dioxirane Reaction mass of 2,2'-{methylenebis[(4,1-phenylene)oxymethylene]}bis(oxirane) and 2-{[4-({2-[(oxiran-2-yl)methoxy]phenyl}methyl)phenoxy]methyl}oxirane and 2,2'-{methylenebis[(2,1-phenylene)oxymethylene]}bis(oxirane) Epoxy Phenol Novolak Resin
Index number in Annex VI of the CLP Regulation:	-
Molecular formula:	Multi constituent substance
Molecular weight or molecular weight range:	<= 700.0
Synonyms	D.E.R.™ 354 Liquid Epoxy Resin EpoTohto YDF-170 EpoTohto YDF-8170 EpoTohto YDF-8170C Epoxy Phenol Novolak Resin

Synonyms, continued:	KD-9005 KD-9009 KDF-438 KSR-177YD-114EF YD-114F YDF-161 YDF-161H YDF-165YDF-170 YDF-175 YDF-2001M75 YDPN-631

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

Structural formula:

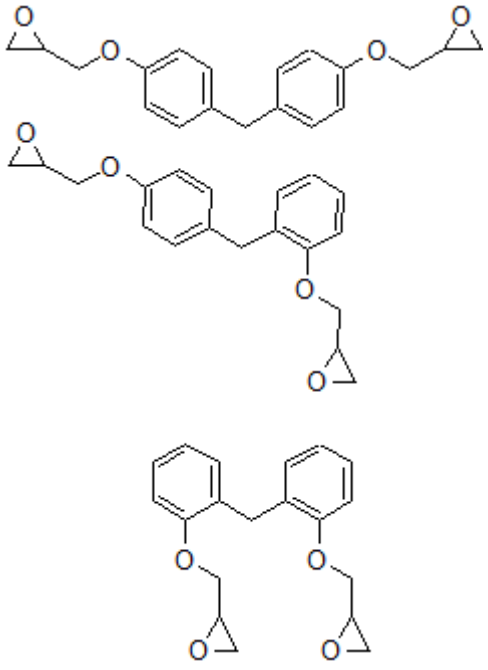
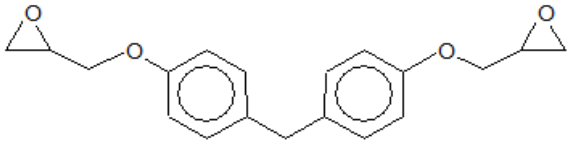
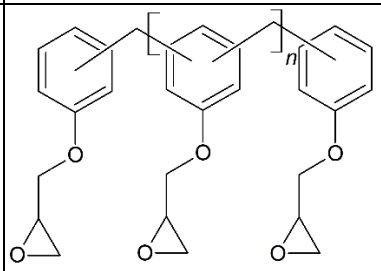
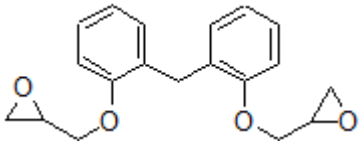
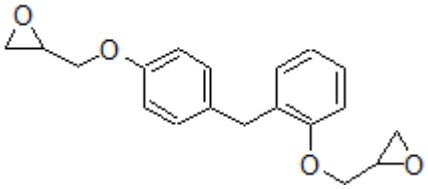


Table: Constituent

Name, CAS number, SMILES	Structural formula
2,2'-[methylenebis(p-phenyleneoxy methylene)]bisoxirane CAS 2095-03-6 EC 218-257-4	
Formaldehyde, oligomeric reaction products with 1-chloro-2,3-epoxypropane and phenol (n = 2-5)	
2,2'-[methylenebis(o-phenyleneoxymethylene)]bisoxirane CAS 54208-63-8 EC 259-026-8	
[[2-[p-(oxiranylmethoxy)benzyl]phenoxy]methyl] oxirane CAS 57469-07-5 EC 260-750-1	

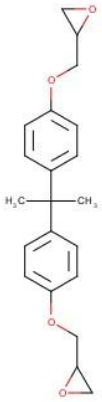
1.2 Similar substances/grouping possibilities

The substance is structurally similar to BPA Epoxy Resin, previously, EC no 500-033-5, following compliance check on SID now EC no 216-823-5, which is under follow-up to substance evaluation from 2015 with DK as the evaluating MSCA.

Table: Similar substance

EC number:	216-823-5
EC name (public):	2,2'-[(1-methylethylidene)bis(4,1-phenyleneoxymethylene)]bisoxirane (previously 4,4'-Isopropylidenediphenol, oligomeric reaction products with 1-chloro-2,3-epoxypropane)
CAS number:	1675-54-3 (previously 25068-38-6)
CAS name (public):	Oxirane, 2,2'-[(1-methylethylidene)bis(4,1-phenyleneoxymethylene)]bis-
IUPAC name (public):	Bis[4-(2,3-epoxy propoxy) phenyl] propane Bisphenol A diglycidyl ether Bisphenol A epoxy resin BADGE
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 regarding the substance EC 500-006-8 was issued by ECHA in 2012 and contained requests for substance ID related information. Following this request, the EC number was updated to 701-263-0.
		☐ Testing proposal
		☐ CoRAP and Substance Evaluation
	Authorisation	☐ Candidate List
		☐ Annex XIV
	Restri -ction	☐ Annex XVII[1]
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)	

[1] Please specify the relevant entry.

(UNEP) Stockholm convention (POPs Protocol)	☐ Assessment
	☐ In relevant Annex
Other processes / EU legislation	☐ Other (provide further details below)

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

Not available for the registered substance. However, for the substance of concern in the first version of this justification document (EC 500-006-8) there are the following self classifications (September 2019)

- 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 for the substance EC 500-006-8:
    - Skin Irrit. 2 H315: Causes skin irritation : 476.
    - Skin Sens. 1 H317: May cause an allergic skin reaction: 482.
    - Eye Irrit. 2 H319: 245
    - Aquatic Chronic 2 H411: Toxic to aquatic life with long lasting effects:485.
    - Aquatic Chronic 4 H413:10
    - Not classified:48

3.1.3 Proposal for Harmonised Classification in Annex VI of the CLP

Not available

4 INFORMATION ON (AGGREGATED) TONNAGE AND USES[2]

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
***the total tonnage band has been calculated by excluding the intermediate uses, for details see the Manual for Dissemination and Confidentiality under REACH Regulation (section 2.6.11): https://echa.europa.eu/documents/10162/22308542/manual_dissemination_en.pdf/7e0b87c2-2681-4380-8389-cd655569d9f0		

4.2 Overview of uses

This substance is used by consumers, in articles, by professional workers (widespread uses), in formulation or re-packing, at industrial sites and in manufacturing.
This substance is used in polymers, modelling clay and semiconducters fillers, putties, plasters, modelling clay, coating products and adhesives and sealants and for non-metal surface treatment products and in paper chemicals and dyes, textile treatment products and dyes and water treatment chemicals.

Table: Uses

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

[2] *The dissemination site was accessed in September 2019.*

5. JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

5.1. Legal basis for the proposal

☒ Article 44(2)

☐ Article 45(5)

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

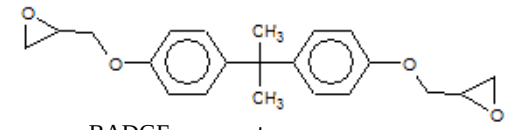
Hazard based concerns		
CMR ☐ C ☐ M ☐ R	Suspected CMR[1] ☐ C ☐ M ☐ R	☒ Potential endocrine disruptor
☐ Sensitiser	☐ Suspected Sensitiser[3]	
☐ PBT/vPvB	☐ Suspected PBT/vPvB[1]	☐ Other (please specify below)
Exposure/risk based concerns		
☐ Wide dispersive use	☐ Consumer use	☐ Exposure of sensitive populations
☐ Exposure of environment	☐ Exposure of workers	☐ Cumulative exposure
☐ High RCR	☐ High (aggregated) tonnage	☐ Other (please specify below)

[3] 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

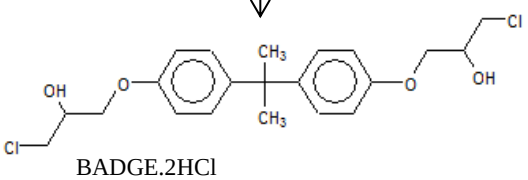
Very limited *in vivo* information is available for endocrine related endpoints for the registered substance. In the registration dossier, read across is performed to the structurally similar substance BADGE (CAS 1675-54-3) to fill the standard information data gap on a two-generation reproductive toxicity 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 evaluated as yet.

A few *in vitro* studies on endocrine related endpoints are recorded from peer reviewed articles for the structurally related substances BADGE and BFDGE 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.

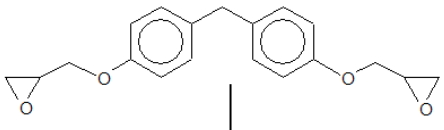
One of the uses of the registered substance is to remove surplus hydrochloric acid in PVC production. The resulting chlorinated transformation products of BADGE and BFDGE have also been tested *in vitro.*



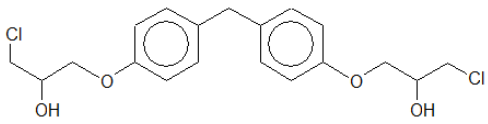
BADGE



BADGE.2HCl



BFDGE



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 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.