Ministry of Environment of Denmark
Environmental Protection Agency

SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

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 No 701-263-0

Evaluating Member State: Denmark

Dated: 27 May 2021

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Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2020

Member State concluded the evaluation without any further need to ask more information from the registrants under Article 46(1) decision.

Further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work. The Community rolling action plan (CoRAP) of substances subject to evaluation, is updated and published annually on the ECHA web site[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the registrant(s) concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the final outcome of the Substance Evaluation carried out by the evaluating Member State. The document consists of two parts i.e. A) the conclusion and B) the evaluation report. In the conclusion part A, the evaluating Member State considers how the information on the substance can be used for the purposes of regulatory risk management such as identification of substances of very high concern (SVHC), restriction and/or classification and labelling. In the evaluation report part B the document provides explanation how the evaluating Member State assessed and drew the conclusions from the information available.

With this Conclusion document the substance evaluation process is finished and the Commission, the Registrant(s) of the substance and the Competent Authorities of the other Member States are informed of the considerations of the evaluating Member State. In case the evaluating Member State proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes. Further analyses may need to be performed which may change the proposed regulatory measures in this document. Since this document only reflects the views of the evaluating Member State, it does not preclude other Member States or the European Commission from initiating regulatory risk management measures which they deem appropriate.

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

Contents

Part A. Conclusion

1. CONCERN(S) SUBJECT TO EVALUATION

The registered substance Reaction mass of 2,2'-[methylenebis(2,1-phenyleneoxy-methylene)]bis(oxirane) and 2,2'-[methylenebis(4,1-phenyleneoxymethylene)]-bis(oxirane) and 2-({2-[4-(oxiran-2-ylmethoxy)benzyl]phenoxy}methyl)oxirane was originally selected for substance evaluation in order to clarify concerns about:

- Endocrine disruption

No additional concerns were identified during the evaluation.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

There are no other completed or ongoing processes relevant for the substance.

3. CONCLUSION OF SUBSTANCE EVALUATION

The evaluation of the available information on the registered substance has led the evaluating member state to the following conclusions, as summarised in the table below.

The registrant has applied read across to the similar substance BADGE (CAS RN 1675-45-3, EC no 216-823-5) to cover the reproductive toxicity endpoint in the REACH registration. Based on an assessment of the read across conducted by the evaluating member state, it is concluded that the read across is unsufficiently justified and that the read across therefore is rejected. The substance is registered at Annex X under REACH and an Extended one-generation reproductive toxicity study (EOGRTS) is a standard information requirement at this tonnage band. The registration dossier does not contain that information and a compliance check should be initiated.

An EOGRTS is a level 5 test under the OECD conceptual framework for testing and assessment of endocrine disruptors defined as an *in vivo* assay providing more comprehensive data on adverse effects on endocrine-relevant endpoints over more extensive parts of the life cycle of the organism. Therefore, this study is assumed to be fundamental in the evaluation of the concern for endocrine disruption, and this evidence will most likely be sufficient to conclude on the endocrine disrupting properties of the substance. It is therefore concluded by the evaluating member state, that the substance should be handed over to ECHA to conduct a compliance check and the substance evaluation should be terminated.

Table 1

CONCLUSION OF SUBSTANCE EVALUATION	
Conclusions	**Tick box**
Need for follow-up regulatory action at EU level	
Harmonised Classification and Labelling	
Identification as SVHC (authorisation)	
Restrictions	
Other EU-wide measures	
No need for regulatory follow-up action at EU level; a compliance check should be initiated.	X

Further information is necessary to inform on the concerns identified by the eMSCA. However, compliance check has been identified as a more expedient process.

Currently no conclusion on the concerns is possible and the substance evaluation is terminated. It is expected that the standard information will be sufficient to clarify the concern on endocrine disruption without further need for information request under substance evaluation. However, should the standard information generated under a dossier evaluation not be sufficient to clarify the concern, a new substance evaluation may be necessary.

4. FOLLOW-UP AT EU LEVEL

4.1. Need for follow-up regulatory action at EU level

Not relevant. Please consult section 3.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

5.1. No need for regulatory follow-up at EU level

Not relevant. Please consult section 3.

5.2. Other actions

In the course of the substance evaluation, the eMSCA identified a data gap in the standard information requirements. This data gap was related to the identified concern. A compliance check should be initiated.

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS (IF NECESSARY)

Indication of a tentative plan is not a formal commitment by the evaluating Member State. A commitment to prepare a REACH Annex XV dossier (SVHC, restrictions) and/or CLP Annex VI dossier should be made via the Registry of Intentions.

Table 2

FOLLOW-UP		
Follow-up action	**Date for intention**	**Actor**
Compliance check	tbd	ECHA
Possible RMOA	tbd	DK
Possible subsequent substance evaluation	tbd	DK

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

The registered substance Reaction mass of 2,2'-[methylenebis(2,1-phenyleneoxy-methylene)]bis(oxirane) and 2,2'-[methylenebis(4,1-phenyleneoxymethylene)]-bis(oxirane) and 2-({2-[4-(oxiran-2-ylmethoxy)benzyl]phenoxy}methyl)oxirane was originally selected for substance evaluation in order to clarify concerns about:

- Endocrine disruption

No additional concerns were identified during the evaluation.

Table 3

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Endocrine disruption	No conclusion can be drawn, as crucial standard information is lacking in the registration dossier. This information should be requested under dossier evaluation and a compliance check should be initiated.

7.2. Procedure

The registered substance was included in CoRAP due to a concern for endocrine disruption and a substance evaluation was initiated in March 2020. The evaluation was targeted towards the endocrine disrupting properties of the substance. Following interactions with the registrant, a read across justification for the applied read across to the similar substance BADGE (CAS RN 1675-45-3, EC no 216-823-5) was provided by the registrant to cover the reproductive toxicity endpoint in the REACH registration. Based on an assessment of the read across conducted by the evaluating member state, it was concluded that the read across is unsufficiently justified and that the read across therefore is rejected. The substance is registered at Annex X under REACH and an Extended one-generation reproductive toxicity study (EOGRTS) is a standard information requirement at this tonnage band. The registration dossier does not contain that information and a compliance check should be initiated.

7.3. Identity of the substance

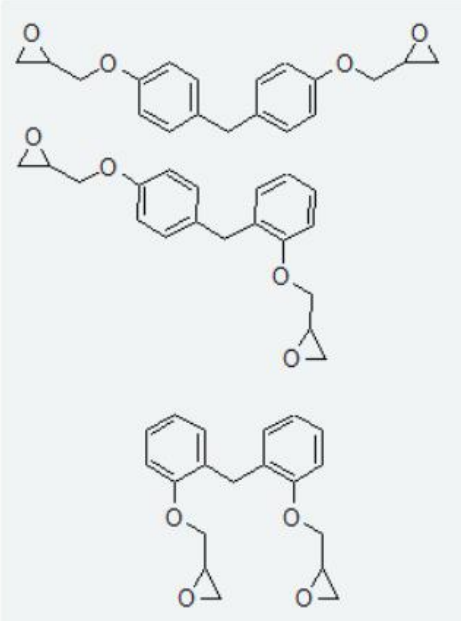
Table 4

SUBSTANCE IDENTITY	
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:	-
Index number in Annex VI of the CLP Regulation:	-
Molecular formula:	C6 H6. C3 H5 Cl . C H2 O)x
Molecular weight range:	-
Synonyms:	D.E.R.™ 354 Liquid Epoxy Resin EpoTohto YDF-170 EpoTohto YDF-8170 EpoTohto YDF-8170C KD-9005 KD-9009 KDF-438 KSR-177 YD-114EF

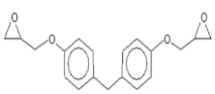
Type of substance ☐ Mono-constituent X Multi-constituent ☐ UVCB

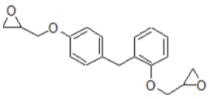
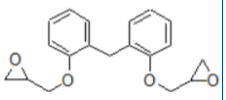
Structural formula:



Multiconstituent/UVCB substance/others

Table 5

Constituent			
Constituents	**Typical concentration**	**Concentration range**	**Remarks**
2,2'-[methylenebis(p-phenyleneoxymethylene)]bisoxirane EC 218-257-4	-	-	

[[2-[p-(oxiranylmethoxy)benzyl]phenoxy]methyl]oxirane EC 260-750-1	-	-	
2,2'-[methylenebis(o-phenyleneoxymethylene)]bisoxirane EC 259-026-8	-	-	

7.4. Physico-chemical properties

Table 6

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	Yellow liquid
Vapour pressure	82 (20°C) and 118 Pa (25°C)
Water solubility	20 mg/L (20°C)
Partition coefficient n-octanol/water (Log Kow)	3.6 (20°C)
Flammability	-
Explosive properties	Non explosive
Oxidising properties	No
Granulometry	-
Stability in organic solvents and identity of relevant degradation products	-
Dissociation constant	-

7.5. Manufacture and uses

7.5.1. Quantities

Table 7

AGGREGATED TONNAGE (PER YEAR)				
☐ 1 – 10 t	☐ 10 – 100 t	☐ 100 – 1000 t	☐ 1000- 10,000 t	☒ 10,000-50,000 t
☐ 50,000 – 100,000 t	☐ 100,000 – 500,000 t	☐ 500,000 – 1000,000 t	☐ > 1000,000 t	☐ Confidential

7.5.2. Overview of uses

Table 8

USES

	Use(s)
Uses as intermediate	-
Formulation	This substance is used in the following products: polymers, coating products, non-metal-surface treatment products and adhesives and sealants. This substance is used in the following activities or processes at workplace: mixing in open batch processes, transfer of substance into small containers, transfer of chemicals, closed batch processing in synthesis or formulation and batch processing in synthesis or formulation with opportunity for exposure. Release to the environment of this substance can occur from industrial use: formulation of mixtures, formulation in materials and as an intermediate step in further manufacturing of another substance (use of intermediates).
Uses at industrial sites	This substance is used in the following products: polymers, coating products, adhesives and sealants, paper chemicals and dyes, textile treatment products and dyes and water treatment chemicals. This substance is used in the following areas: building & construction work. This substance is used for the manufacture of: chemicals, machinery and vehicles, electrical, electronic and optical equipment, plastic products and fabricated metal products. This substance is used in the following activities or processes at workplace: mixing in open batch processes, transfer of chemicals, transfer of substance into small containers, closed batch processing in synthesis or formulation, industrial spraying, calendering operations, closed, continuous processes with occasional controlled exposure, treatment of articles by dipping and pouring and roller or brushing applications. Release to the environment of this substance can occur from industrial use: in the production of articles, in processing aids at industrial sites, as an intermediate step in further manufacturing of another substance (use of intermediates) and as processing aid.
Uses by professional workers	This substance is used in the following products: polymers, coating products, adhesives and sealants, fillers, putties, plasters, modelling clay and semiconductors. This substance is used in the following areas: building & construction work and formulation of mixtures and/or re-packaging. This substance is used for the manufacture of: plastic products, machinery and vehicles, electrical, electronic and optical equipment, fabricated metal products and mineral products (e.g. plasters, cement). This substance is used in the following activities or processes at workplace: transfer of chemicals, hand mixing with intimate contact only with personal protective equipment available, roller or brushing applications, non-industrial spraying, mixing in open batch processes, closed, continuous processes with occasional controlled exposure, treatment of articles by dipping and pouring and transfer of substance into small containers.

	Other release to the environment of this substance is likely to occur from: indoor use (e.g. machine wash liquids/detergents, automotive care products, paints and coating or adhesives, fragrances and air fresheners) and outdoor use.
Consumer Uses	This substance is used in the following products: fillers, putties, plasters, modelling clay, coating products and adhesives and sealants. Other release to the environment of this substance is likely to occur from: indoor use (e.g. machine wash liquids/detergents, automotive care products, paints and coating or adhesives, fragrances and air fresheners) and outdoor use.
Article service life	This substance is used in the following activities or processes at workplace: high energy work-up of substances bound in materials or articles (e.g. hot rolling/forming, grinding, mechanical cutting, drilling or sanding), production of mixtures or articles by tabletting, compression, extrusion or pelletisation, roller or brushing applications, non-industrial spraying and the low energy manipulation of substances bound in materials or articles. Release to the environment of this substance can occur from industrial use: of articles where the substances are not intended to be released and where the conditions of use do not promote release and industrial abrasion processing with low release rate (e.g. cutting of textile, cutting, machining or grinding of metal). Other release to the environment of this substance is likely to occur from: indoor use in long-life materials with low release rate (e.g. flooring, furniture, toys, construction materials, curtains, foot-wear, leather products, paper and cardboard products, electronic equipment) and outdoor use in long-life materials with low release rate (e.g. metal, wooden and plastic construction and building materials). This substance can be found in complex articles, with no release intended: machinery, mechanical appliances and electrical/electronic products (e.g. computers, cameras, lamps, refrigerators, washing machines) and vehicles. This substance can be found in products with material based on: metal (e.g. cutlery, pots, toys, jewellery) and plastic (e.g. food packaging and storage, toys, mobile phones).

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

There are no harmonised classifications for the registered substance.

7.6.2. Self-classification

- In the registration(s):

  Skin Irrit. 2; H315
  Skin Sens. 1; H317
  Aquatic Chronic 2; H411

- There are no further hazard classes notified among the aggregated self-classifications in the C&L Inventory.

7.7. Environmental fate properties

The environmental fate properties have not been evaluated by eMSCA in this substance evaluation.

7.8. Environmental hazard assessment

An environmental hazard assessment has not been performed by the eMSCA in this substance evaluation.

7.9. Human Health hazard assessment

7.9.1. Toxicokinetics

Not evaluated by the eMSCA in this substance evaluation.

7.9.2. Acute toxicity and Corrosion/Irritation

Not evaluated by the eMSCA in this substance evaluation.

7.9.3. Sensitisation

Not evaluated by the eMSCA in this substance evaluation.

7.9.4. Repeated dose toxicity

Not evaluated by the eMSCA in this substance evaluation.

7.9.5. Mutagenicity

Not evaluated by the eMSCA in this substance evaluation.

7.9.6. Carcinogenicity

Not evaluated by the eMSCA in this substance evaluation.

7.9.7. Toxicity to reproduction (effects on fertility and developmental toxicity)

The registrant has applied read across to the similar substance BADGE (EC no 216-823-5, CAS RN 1675-45-3) to cover the reproductive toxicity endpoint in the REACH registration. Based on an assessment of the read across conducted by the evaluating member state, it is concluded that the read across is unsufficiently justified and that the read across therefore is rejected. Therefore, eMSCA concludes that a data gap exists for this substance.

7.9.8. Hazard assessment of physico-chemical properties

Not evaluated by the eMSCA in this substance evaluation.

7.9.9. Selection of the critical DNEL(s)/DMEL(s) and/or qualitative/semi-quantitative descriptors for critical health effects

Not evaluated by the eMSCA in this substance evaluation.

7.9.10. Conclusions of the human health hazard assessment and related classification and labelling

Conclusion cannot be made since the endocrine disruption concern is unresolved.

7.10. Assessment of endocrine disrupting (ED) properties

7.10.1. Endocrine disruption – Environment

The endocrine disrupting properties in the environment have not been assessed in this substance evaluation.

7.10.2. Endocrine disruption - Human health

The registered substance was included in the CoRAP list due to a concern for endocrine disruption. The concern was based on the following:

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 was 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*. 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. Consequently 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.

Very limited *in vivo* information is available for endocrine related endpoints for the registered substance. In the registration dossier, the registrant has used read across to a two-generation reproductive toxicity study (OECD TG 416) conducted on the structurally similar substance BADGE (CAS RN 1675-54-3) to fill the standard information requirement for a reproductive toxicity. 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.

7.10.3. Conclusion on endocrine disrupting properties

The registrant has applied read across to the similar substance BADGE (EC no 216-823-5, CAS RN 1675-45-3) to cover the reproductive toxicity endpoint in the REACH registration. Based on an assessment of the read across conducted by the evaluating member state, it is concluded that the read across is unsufficiently justified and that the read-across therefore is rejected.

The Substance is registered at Annex X under REACH and an Extended one-generation reproductive toxicity study (EOGRTS) is a standard information requirement at this tonnage band. The registration dossier does not contain that information and a compliance check should be initiated.

It is not possible to conclude on the endocrine disrupting properties of the registered substance based on the currently available data.

7.11. PBT and VPVB assessment

The PBT/vPvB properties of the registered substance have not been assessed by eMSCA in this substance evaluation.

7.12. Exposure assessment

An exposure assessment has not been conducted for the registered substance by eMSCA in this substance evaluation.

7.13. Risk characterisation

A risk characterisation has not been conducted by eMSCA for the registered substance in this substance evaluation.

7.14. References

Nakazawa, H., Yamaguchi, A., Yamazaki, T., Kato, K., Yoshimura, Y. and Makino, T. (2002). In vitro assay of hydrolysis and chlorohydroxy derivatives of bisphenol A diglycidyl ether for estrogenic activity, Food and Chemical Toxicology, Vol. 40, issue 12, pp. 1827-1832. DOI: https://doi.org/10.1016/S0278-6915(02)00165-5

Satoh, K., Ohyama, K., Aoki, N., Iida, M. and 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, Vol. 42, issue 6, pp. 983-993. DOI: https://doi.org/10.1016/j.fct.2004.02.011

7.15. Abbreviations

AR: Androgen receptor

BADGE: Bisphenol A diglycidyl ether (EC no 216-823-5, CAS RN 1675-45-3)

BFDGE: Bisphenol F diglycidyl ether

CoRAP: Community rolling action plan

eMSCA: Evaluating Member State Competent Authority

EOGRTS: Extended one-generation reproductive toxicity study

ER: Estrogen receptor

HCL: Hydrogen chloride

MS: Member state

OH: Hydroxide

Tbd: To be decided