Bundesanstalt für Arbeitsschutz
und Arbeitsmedizin
Federal Institute for Occupational
Safety and Health

SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

1,3-dioxolane

EC No 211-463-5

CAS RN 646-06-0

Evaluating Member State(s): Germany

Dated: May 2022

Evaluating Member State Competent Authority

BAuA
Federal Institute for Occupational Safety and Health
Division 5 - Federal Office for Chemicals
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Year of evaluation in CoRAP: 2016

Before concluding the substance evaluation, a Decision to request further information was issued on 16 December 2019

Further information on registered substances here:

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

DISCLAIMER

This document has been prepared by the evaluating Member State as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating Member State nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

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 Substance (1,3-dioxolane, EC number 211-463-5) was originally selected for substance evaluation[2] (SEv) in order to clarify concerns about:

- Mutagenicity,
- Reproductive toxicity and
- Consumer exposure.

During the evaluation also other concerns were identified. The additional concerns were:

- Narcotic effects,
- Skin irritation,
- Serious eye damage and
- Professional (worker) exposure.

2 OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

In 2020, the eMSCA initiated a Regulatory Management Option Analysis (RMOA) for the Substance 1,3-dioxolane and other solvents (conclusion expected in 2022), focussing on product features in combination with information on the concentrations of the respective substances in consumer products.

In 2019, the registrants submitted a harmonised classification and labelling (CLH) dossier to ECHA with a proposal to update the existing classification of the substance 1,3-dioxalane as Flam. Liq. 2, H225 with Eye Dam. 1, H318 (Causes serious eye damage) and Repr. 1B, H360D (May damage the unborn child). The CLH dossier was not resubmitted by the registrants following the ECHA's accordance check (2019) and it is therefore listed on ECHA's registry of intention with no further information[3].

In addition, two dossier evaluations (CCHs) were performed by ECHA on the substance 1,3-dioxolane. Following the first one, the registrants submitted an *in vitro* gene mutation study in bacteria (OECD TG 471) and a PNDT study in rabbits (OECD TG 414) in 2015 and 2017, respectively.[4] The latest CCH (2021)[5] requested an Extended One-Generation Reproductive Toxicity Study (EOGRTS), which is currently being performed and expected in April 2024.

[2] https://echa.europa.eu/documents/10162/bba80f18-dfa3-7695-c323-26d8ddbac7b2
[3] https://echa.europa.eu/registry-of-clh-intentions-until-outcome/-/dislist/details/0b0236e183bf910a
[4] https://echa.europa.eu/documents/10162/1f1fee33-2a70-e6a0-a32a-bee7fd6b699a
[5] https://echa.europa.eu/documents/10162/7f5478d4-256b-22a7-2972-3250029a092c

3 CONCLUSION OF SUBSTANCE EVALUATION

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

Table 1

Conclusion of substance evaluation	
Conclusions	**Tick box**
Need for follow-up regulatory action at EU level	X
Harmonised Classification and Labelling	X
Identification as SVHC (authorisation)	
Restrictions	
Other EU-wide measures	
No need for regulatory follow-up action at EU level	

4 FOLLOW-UP AT EU LEVEL

4.1 Need for follow-up regulatory action at EU level

A Regulatory Management Option Analysis (RMOA) by the eMSCA is currently ongoing for the substance 1,3-dioxolane and will be finalised in 2022. In an EU-wide consultation as part of this process, the eMSCA aims at obtaining a better understanding of the variety of consumer products with solvents on the market (including for the substance 1,3-dioxolane) to enable more realistic exposure estimation and risk assessment.

For the professional user, risks to human health have been identified which could potentially be addressed by a restriction. However, this is still subject to further assessment. In addition, risks related to narcotic effects, effects on the blood system/immune system and reprotoxicity effects cannot be ruled out for consumers. The preliminary assessments of the eMSCA are based on general information on typical product characteristics. Detailed information about the products and their applications is currently missing. The eMSCA is particularly interested in an exchange with companies and stakeholders who are familiar with solvent-based consumer products. These include formulators, product developers and end users, as well as fabric manufacturers, importers, distributors/dealers, associations, NGOs and interested third parties.

In addition, market inquiries at the national level are ongoing for paint removers, adhesives and sealants. These inquiries complement the consultation and provide exposure-relevant data. In addition, consumer surveys are ongoing or initiated to generate data that can be used to evaluate and possibly substantiate the exposure estimation, in particular for the consumer use of adhesives and paint removers.

The RMOA will determine whether 1,3-dioxolane poses a health risk to consumers, whether further risk management measures are necessary for the use of consumer products, and which measure(s) can be considered best suited in order to minimise the potential risk for the consumer.

4.1.1 Harmonised Classification and Labelling

Available data indicate that the substance 1,3-dioxolane meets the criteria for classification as STOT SE 3, H336 (May cause drowsiness or dizziness) and Eye Dam. 1, H318 (Causes serious eye damage).
Observed effects in foetuses of rats and rabbits after prenatal treatment with the substance 1,3-dioxolane are indicative of the need for classification of the substance 1,3-dioxolane for developmental toxicity, but data may not be sufficient for an appropriate sub-categorisation (i.e., Repr. 1B, H360D vs. Repr. 2, H361d). Classification criteria of Category

2 seem to be fulfilled, whereas effects may be considered borderline for Category 1B. In addition, once the results of the EOGRTS requested under dossier evaluation (CCH) is available (anticipated for April 2024), a decision on the appropriate sub-categorisation for this hazard class and an assessment of assess potential effects of the Substance on sexual function, fertility and developmental immunotoxicity can be made. Subsequently, the eMSCA is ready to initiate a respective harmonised classification and labelling (CLH) process. In case it is decided to submit a CLH proposal for the substance 1,3-dioxolane, the hazard classes STOT SE 3 (narcotic effects) and Eye Dam. will be addressed as well.

4.1.2 Identification as a substance of very high concern, SVHC (first step towards authorisation)

Not applicable.

4.1.3 Restriction

Not applicable.

4.1.4 Other EU-wide regulatory risk management measures

Not applicable.

5 CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

5.1 No need for regulatory follow-up at EU level

Not applicable.

5.2 Other actions

Not applicable.

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
CLH dossier depending on outcome of the EORGTS (currently requested in a CCH) – for details see 4.1.1 and 7.9.7	End 2024	DE CA
Ongoing RMOA (risks to consumers)	End 2022	DE CA

Part B. Substance evaluation

7 EVALUATION REPORT

7.1 Overview of the substance evaluation performed

The Substance (1,3-dioxolane, EC number 211-463-5) was originally selected for substance evaluation[6] (SEv) in order to clarify concerns about:

- Mutagenicity,
- Reproductive toxicity and
- Consumer exposure.

During the evaluation also other concerns were identified. The additional concerns were:

- Narcotic effects,
- Skin irritation,
- Serious eye damage and
- Professional (worker) exposure.

Table 3

Evaluated endpoints	
Endpoint evaluated	**Outcome / conclusion**
Mutagenicity	Concern refuted. 1,3-dioxolane does not need to be classified for mutagenicity. No further action required.
Reproductive toxicity (developmental toxicity)	Concern confirmed. Developmental toxicity in rabbits. Harmonised classification process to be initiated. Note: Developmental immunotoxicity concern may be clarified from Cohort 3 of the ongoing EOGRTS.
Reproductive toxicity (sexual function and fertility)	Concern unresolved. Ongoing EOGRTS. The eMSCA is ready to reassess this endpoint upon submission of the additional data to conclude on the need for harmonised classification for this endpoint. Harmonised classification process to be initiated.
Consumer Exposure	Concern unresolved. Risks cannot be ruled out for consumers. Ongoing RMOA to further assess the risk arising from consumer uses of 1,3-dioxolane. The ongoing EOGRTS may affect the level of PoD/DNELs needed for the risk characterisation.
Narcotic effects (STOT SE 3) (STOT SE 1 and 2)	Concern confirmed. Specific Target Organ Toxicity, Single Exposure, Category 3, i.e., STOT SE 3, H336 (May cause drowsiness and dizziness), appears to be justified. Harmonised classification process to be initiated. Based on the available data assessed so far, no indication for STOT SE 1 or 2 was identified.
Skin irritation/corrosion	Concern refuted. No further action is required.
Eye irritation/serious eye damage	Concern confirmed.

[6] https://echa.europa.eu/documents/10162/bba80f18-dfa3-7695-c323-26d8ddbac7b2

Evaluated endpoints	
Endpoint evaluated	**Outcome / conclusion**
	1,3-dioxolane must be classified as Eye Dam. 1, H318 (Causes serious eye damage). Harmonised classification process to be initiated.
Professional (worker) exposure	Concern confirmed. A risk for the professional user cannot be excluded. Assessment to be completed in a RMOA potentially followed by a restriction.
Additional endpoints evaluated	
Toxicokinetics	Default value of 100 % for the oral, dermal and inhalation absorption, respectively.
Acute Toxicity	1,3-Dioxolane does not need to be classified for Acute Tox.
Skin Sensitisation	1,3-dioxolane does not cause skin sensitisation. No further action required.
Repeated Dose Toxicity	Repeated dose toxicity effects (blood system, immune system) do not justify classification. No further action required.
Carcinogenicity	No carcinogenicity potential based on a weight of evidence of available data. Currently no further action required. Note: 1,3-Dioxolane may contain formaldehyde. CLP mixture rules may apply for self-classification.

7.2 Procedure

The substance 1,3-dioxolane was originally selected in 2016 for substance evaluation[7] in order to clarify various concerns as detailed in section 7.1.

The following endpoints were subject to the evaluation: acute toxicity, eye irritation/damage and skin irritation/corrosion, specific target organ toxicity after single exposure (respiratory tract irritation and narcotic effects), skin sensitisation, specific target organ toxicity after repeated or prolonged exposure, mutagenicity, carcinogenicity and reproductive toxicity. In addition, consumer exposure was assessed.

The evaluation was based on the original data from registration dossiers, on the available US EPA HPV Challenge Program Submission for 1,3-dioxolane, on MAK evaluations for occupational health and safety for 1,3-dioxolane, publicly available scientific publications, and study reports that were provided by the registrants. A literature search was performed for 1,3-dioxolane before the start of the evaluation process and identified literature was compared to references cited in the registration dossiers. For the exposure assessment also secondary sources like national product data bases and measurements, Safety Data Sheets, as well as published journal articles and reports were considered.

During the initial 12-months evaluation period, the eMSCA entered into a dialogue with the registrants in order to retrieve more information and reduce uncertainties regarding products on the market and their uses. A revised consumer exposure assessment and risk characterisation was provided to the eMSCA in September 2016. However, it cannot be concluded with sufficient certainty that the operational conditions in the CSRs cover the situation on the market.

In 2020, the eMSCA initiated a RMOA for 1,3-dioxolane and other solvents, focussing on product features in combination with information on the concentrations of the respective substances in consumer products. After finalisation of the RMOA (expected in 2022) it

[7] https://echa.europa.eu/documents/10162/bba80f18-dfa3-7695-c323-26d8ddbac7b2

should be clear whether 1,3-dioxolane poses a health risk to consumers and whether and which further risk management measures are necessary for the use of consumer products.

A Substance Evaluation Decision[8] was sent to the registrants in December 2019, requesting *in vitro* studies with respect to the endpoints skin irritation and serious eye damage. The respective data were submitted by the registrant(s) in 2021 and made available as robust study summaries.

During the substance evaluation process, an *in vitro* gene mutation study in bacteria (OECD TG 471) and a PNDT study in rabbits (OECD TG 414) were provided by the registrants in 2015 and 2017, respectively, upon dossier evaluation[9]. These data were included in the hazard assessment by the eMSCA.

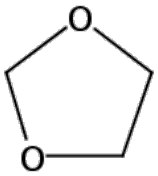
7.3 Identity of the substance

Table 4

SUBSTANCE IDENTITY	
Public name:	1,3-dioxolane
EC number:	211-463-5
CAS number:	646-06-0
Index number in Annex VI of the CLP Regulation:	605-017-00-2
Molecular formula:	$C_3H_6O_2$
Molecular weight range:	74.08 g/mol
Synonyms:	▫ 1,3-Dioxacyclopentane ▫ 1,3-Dioxole, dihydro- ▫ Dioxolane ▫ Ethylene glycol formal ▫ Formal glycol ▫ Glycolformal

Type of substance: Mono-constituent

Structural formula:



[8] https://echa.europa.eu/documents/10162/33ddf770-fbcc-2cb2-1e22-706273e85c77

[9] https://echa.europa.eu/documents/10162/1f1fee33-2a70-e6a0-a32a-bee7fd6b699a

7.4 Physico-chemical properties

Table 5

Overview of physicochemical properties	
Property	**Value**
Physical state at 20 °C and 101.3 kPa	Clear colourless liquid
Vapour pressure	10100 Pa (20 °C)
Water solubility	Completely miscible in water
Partition coefficient n-octanol/water (Log Kow)	-0.37 (20 °C)
Flashpoint	-5 °C (Closed cup), GESTIS database on hazardous substances base (IFA)
Autoflammability Auto-ignition temperature	245 °C, GESTIS database on hazardous substances base (IFA)
Lower explosion limit	2.3 vol%, GESTIS database on hazardous substances base (IFA)
Upper explosion limit	30.5 vol%, GESTIS database on hazardous substances base (IFA)
Flammability Flammability upon ignition (solids) Flammability in contact with water and pyrophoric properties	1,3-Dioxolane does not form flammable gases in contact with water and has no pyrophoric properties.
Explosive properties	Non-explosive
Oxidising properties	Non-oxidising
Granulometry	Not applicable
Stability in organic solvents and identity of relevant degradation products	In accordance with Column 2 of REACH Annex VII, information is only required if stability of the substance is considered to be critical. For 1,3-dioxolane, the stability is not critical, therefore no additional information needs to be provided.
Dissociation constant	No dissociation properties, no pKa values within range of 2 to 11 (pKa < 2)
Melting point	-95 °C (at 1014 hPa)
Boiling point	76 °C (at 1014 hPa)
Relative density	1.06 (20 °C)

7.5 Manufacture and uses

7.5.1 Quantities

Table 6

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	☒ > 1000 t

7.5.2 Overview of uses

1,3-Dioxolane is used at industrial sites and in manufacturing, in formulation or re-packing, by professional workers (including widespread and wide dispersive uses), and by consumers.

1,3-Dioxolane is mainly used for the manufacture of polymers or as part of plastic products (as a monomer bound in polymers). 1,3-Dioxolane serves as a co-monomer in the manufacturing of polyoxymethylene (POM) but also serves as an aprotic solvent in the manufacturing process of other polymers, as it shows high degrees of solubility for polar polymers (e.g., polyurethanes, polyesters, epoxides, PVCs). As the manufacture of polymers takes place at industrial sites where adequate exposure control measures are supposed to be at place, the exposure situation can be considered adequately controlled for this type of setting.

In addition, 1,3-dioxolane is also used as a typical solvent for a wide range of wide dispersive uses and products (other than polymers) which are also registered, such as coatings and paints, thinners and paint removers, washing and cleaning products, anti-freeze and de-icing products, lubricants, greases and release products, and hydraulic fluids.

However, the amount of 1,3-dioxolane used for these applications, other than polymer production, is only a minor fraction of the overall market volume: the total tonnage registered for uses as a solvent (other than in polymer production) for 2018 was just above 3 000 tonnes. (For comparison: ethyl acetate or acetone as examples for typical solvents that are large volume chemicals are both registered with tonnage bands of 100 000 – 1 000 000 tonnes per annum). This indicates that 1,3-dioxolane can be seen more as a speciality chemical used in special products with low market volumes rather than a commodity chemical.

Table 7 provides an overview of the uses according to ECHA's dissemination site[10] (as per January 2022). All listed uses are included.

Table 7

USES	Use(s)
Manufacture	- Manufacture/Polyoxymethylene (ER: Manufacture of the substance) (PROC 2) - Manufacture (ERC1: Manufacture of the substance) (PROC 1, 3, 8a, 8b) - Manufacture (ERC1: Manufacture of the substance) (PROC 1, 2, 3, 4, 8a, 8b, 15)
Formulation	- Formulation (ERC2: Formulation into mixture) (PROC 1, 2, 3, 4 (indoor), 4 (outdoor), 5, 8a (indoor), 8a (outdoor), 8b (indoor), 8b (outdoor, 9 (indoor), 9 (outdoor), 14, 15) - Formulation (ERC3: Formulation into solid matrix) (PROC 3, 4, 5, 6, 14) - Formulation (ERC2: Formulation into mixture) (PROC 1, 2, 3, 4, 8a, 8b, 9, 15) (PC 21: Laboratory chemicals) - Distribution (ERC2: Formulation into mixture) (PROC 1, 2, 3, 4, 8a, 8b, 9, 15) - Formulation of preparations (ERC2: Formulation into mixture) (PROC 1, 2, 3, 5) - Formulation of preparations, professional (ERC2: Formulation into mixture) (PROC 3, 5)
Uses at industrial sites	- Use in industrial chemical processes (ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article)) (PROC 1, 2, 3) - Polymerisation (ERC6c: Use of monomer in polymerisation processes at industrial site (inclusion or not into/onto article)) (PROC 1, 2, 3, 4, 5, 8b, 14, 15) (PC 32: Polymer preparations and compounds)

[10] https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15807/3/1

USES	Use(s)
	- Use as monomer (ERC6c: Use of monomer in polymerisation processes at industrial site (inclusion or not into/onto article)) (PROC 2) (PC 32: Polymer preparations and compounds) - Use at industrial site in coating (ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article) (PROC 5, 7, 8a, 8b, 9, 10, 13) (PC 9a: Coatings and paints, thinners, paint removes) - Use at industrial site in cleaning agent (ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article) (PROC 7, 8a, 8b, 10, 13) (PC 35: Washing and cleaning products) - Use in laboratories (ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article)) (PROC 15) - Production of polymer pallets [sic] and flakes (ERC6c: Use of monomer in polymerisation processes at industrial site (inclusion or not into/onto article)) (PROC 1, 8a, 8b) (PC 32: Polymer preparations and compounds) - Use at industrial site in intermediate (ERC6a: Use of intermediate) (PROC 1, 2, 3, 4, 8a, 8b, 15) - Production of polymer pallets [sic] and flakes (ERC6c: Use of monomer in polymerisation processes at industrial site (inclusion or not into/onto article)) (PROC 1) (PC 19: Intermediate) - Use at industrial site in metal working fluid/rolling oils (ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article)) (PROC 5, 7, 8a, 8b, 9, 10, 13, 17) (PC 17: Hydraulic fluids) - Use at industrial site in coating (ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article)) (PROC 5, 7, 8a, 8b, 10, 13, 15) (PC 9a: Coatings and paints, thinners, paint removes) - Use at industrial site in laboratory applications (ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article)) (PROC 10, 15) (PC 21: Laboratory chemicals) - Charging and discharging of substances and mixtures (ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article)) (PROC 8a, 8b, 9) - Use at industrial site in cleaning agent (ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article) (PROC 2, 3, 4, 7, 8a, 8b, 10, 13) (PC 35: Washing and cleaning products) - Use in coatings (ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article)) (PROC 1, 2, 3, 4, 5, 7, 8a, 8b, 10, 13) (PC 9a: Coatings and paints, thinners, paint removes) - Use at industrial site in lubricants (ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article) (PROC 5, 7, 8a, 8b, 9, 10, 13, 17, 18) (PC 24: Lubricants, greases, release products) - Polymerization of 1,3-dioxolane (ERC6c: Use of monomer in polymerisation processes at industrial site (inclusion or not into/onto article)) (PROC 1, 8a, 8b) - Monomer in imported polymer (PROC 0) (PC 19: Intermediate) - Use at industrial site in polymer processing (ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article)) (PROC 1, 2, 3, 4, 5, 6, 8a, 8b, 9, 13, 14) (PC 32: Polymer preparations and compounds) - Monomer in a polymer backbone (ERC5: Use at industrial site leading to inclusion into/onto article) (PROC 1, 0) (PC 32: Polymer preparations and compounds) - Production of polymer pallets [sic] and flakes (ERC6c: Use of monomer in polymerisation processes at industrial site (inclusion or not into/onto article)) (PROC 1, 9) (PC 32: Polymer preparations and compounds) - Polymerization of 1,3-dioxolate (ERC6c: Use of monomer in polymerisation processes at industrial site (inclusion or not into/onto article)) (PROC 1, 8a, 8b) - Polymerisation process (ERC6c: Use of monomer in polymerisation processes at industrial site (inclusion or not into/onto article)) (PROC 1, 2, 3, 4, 5, 8a, 8b, 14, 15) (PC 32: Polymer preparations and compounds) - Use at industrial site in binders and release agents (ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article) (PROC 6, 7, 8b, 10, 13, 14)
Uses by professional workers	- Use as laboratory chemical (ERC8c: Widespread use leading to inclusion into/onto article (indoor)) (PROC 15) (PC 32: Polymer preparations and compounds)

USES	Use(s)
	- Use by professional worker in binders and release agents (ERC8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor) / ERC8d: Widespread use of non-reactive processing aid (no inclusion into or onto article, outdoor)) (PROC 6, 8a, 8b, 10, 11, 14) - Use by professional worker in metal working fluid/rolling oils (ERC8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor)) (PROC 5, 8a, 8b, 10, 11, 13, 17) (PC 17: Hydraulic fluids) - Use by professional worker in de-icing agent (ERC8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor) / ERC8d: Widespread use of non-reactive processing aid (no inclusion into or onto article, outdoor)) (PROC 8b, 10, 11) (PC 4: Anti-freeze and de-icing products) - Use by professional worker in cleaning agent (ERC8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor) / ERC8d: Widespread use of non-reactive processing aid (no inclusion into or onto article, outdoor)) (PROC 8a, 8b, 10, 11, 13) (PC 35: Washing and cleaning products) - Use by professional worker in coating (ERC8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor) / ERC8d: Widespread use of non-reactive processing aid (no inclusion into or onto article, outdoor)) (PROC 5, 8a, 8b, 9, 10, 11, 13, 15) (PC 9a: Coatings and paints, thinners, paint removes) - Use as laboratory chemical (ERC8c: Widespread use leading to inclusion into/onto article (indoor)) (PROC 15) (PC 32: Polymer preparations and compounds) - Use by professional worker in polymer processing (ERC8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor)) (PROC 1, 2, 6, 8a, 8b, 14) (PC 32: Polymer preparations and compounds) - Use in laboratories, professional (ERC8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor) (PROC 15) - Charging and discharging of substances and mixtures, professional (ERC8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor) (PROC 8a, 8b, 9) - Use by professional worker in lubricants (ERC8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor)) (PROC 5, 8a, 8b, 9, 10, 11, 13, 17, 18, 20) (PC 24: Lubricants, greases, release products) - Use by professional worker in laboratory applications (ERC8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor)) (PROC 10, 15) (PC 21: Laboratory chemicals) - Use in industrial chemical processes, professional (ERC8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor) / ERC8d: Widespread use of non-reactive processing aid (no inclusion into or onto article, outdoor)) (PROC 1, 2, 3)
Consumer Uses	Use in coatings: PC 1: Adhesives, sealants PC 9a: Coatings and paints, thinners, paint remover PC 15: Non-metal-surface treatment products PC 23: Leather tanning, dye, finishing, impregnation and care products PC 24: Lubricants, greases, release products Use in cleaning agents: PC 9a: Coatings and paints, thinners, paint remover PC 24: Lubricants, greases, release products PC 35: Washing and cleaning products (including solvent based products) Use as lubricant: PC 1: Adhesives, sealants PC 24: Lubricants, greases, release products Use as a cosmetics: PC 28: Perfumes, fragrances PC 39: Cosmetics (Personal care products)
Article service life	Not applicable (under this section, the dissemination site references use of the substance as “monomer in imported polymers” handled by workers, albeit with the note that polymers do not constitute articles).

7.6 Classification and Labelling

7.6.1 Harmonised Classification (Annex VI of CLP)

Table 8

Harmonised Classification according to Annex VI of CLP Regulation (Regulation (EC) 1272/2008)							
Index No	International Chemical Identification	EC No	CAS No	Classification		Spec. Conc. Limits, M-factors	Notes
				Hazard Class and Category Code(s)	Hazard statement code(s)		
605-017-00-2	1,3-dioxolane	211-463-5	646-06-0	Flam. Liq. 2	H225		

7.6.2 Self-classification

In the registrations, two sets of self-classifications are reported.

First Set:

- Flam. Liq. 2: H225 (Highly flammable liquid and vapour)
- Eye Dam.1: H318 (Causes serious eye damage)

Second Set, including hazard classes that are in addition notified among the aggregated self-classifications in the C&L Inventory:

- Repr. 1B: H360 (May damage fertility or the unborn child). The majority of notifications further specify H360D, i.e. developmental toxicity, as well as the oral route.
- Eye Irrit. 2, H319 (Causes serious irritation)

7.7 Environmental fate properties

Not assessed as part of this substance evaluation.

7.8 Environmental hazard assessment

Not assessed as part of this substance evaluation.

7.9 Human Health hazard assessment

7.9.1 Toxicokinetics

No guideline-conform experimental toxicokinetic studies in animals or any relevant human data are available for 1,3-dioxolane. Two toxicokinetic studies of limited reliability from the scientific literature are available, testing the substance in dogs via the inhalation route (Dahl et al., 1991; Snipes et al., 1991). However, as the test system used has not been validated so far, and as only one concentration was tested, only a very low number of test animals was included (n = 3), and only one species was tested, the results of both studies were overall considered insufficiently reliable for a robust risk assessment.

The physicochemical properties of 1,3-dioxolane, namely the high-water solubility (‘*completely miscible in water’)*, the log P of -0.37 (measured at 20 °C) and the low molecular weight (74.08 g/mol), indicate that the substance is favourable for absorption via the inhalation, oral and dermal routes. Thus, from the physicochemical data and the available toxicokinetic and toxicity studies with 1,3-dioxolane, the eMSCA considers that

there are no reasons to deviate from the default value of 100 % for oral, dermal and inhalation absorption for risk assessment.

7.9.2 Acute Toxicity

7.9.2.1 Acute oral, dermal and inhalation toxicity

The registrants concluded that 1,3-dioxolane **does not need to be classified for Acute Tox. via the oral, dermal and the inhalation route**, and based on the available information (i.e. LD50s > 2000 mg/kg bw/d and LC50 > 20.0 mg/L), the eMSCA supports this conclusion.

7.9.2.2 Effects after single exposure

Based on changes of a transient nature in neurobehavioural function consistent with CNS depression observed in the available acute and chronic animal studies (inhalation and oral route) and supported by some information found for humans, the eMSCA concludes that for 1,3-dioxolane the **criteria for classification and labelling for STOT SE category 3 for narcotic effects are fulfilled** according to the CLP Regulation (Annex I, Part 3.8.2.2.2). Thus, classification of 1,3-dioxolane as STOT SE 3, H336 (May cause drowsiness or dizziness) is considered justified.

From the available animal data, a NOAEL of 750 mg/kg bw for narcotic effects after single oral substance administration (Argus Research Laboratories, 1991b) and a NOAEC of 7.0 mg/L for narcotic effects after acute inhalation (Toxicology Research Laboratory, 1989) can be derived. The eMSCA considers that classification as STOT SE 1 or 2 is not supported.

7.9.2.3 Skin corrosion / irritation

In the SEv Decision, an *in vitro* skin irritation test (i.e. OECD TG 439) was requested to allow for a substantiated hazard assessment. Based on the results of the available and the recently provided negative *in vitro* skin irritation study, it is concluded that 1,3-dioxolane is not a skin irritant and **does not need to be classified for Skin Irrit. according to CLP**.

7.9.2.4 Serious eye damage / eye irritation

In the SEv Decision on 1,3-dioxolane, an *in vitro* test for identifying i) chemicals inducing serious eye damage and ii) chemicals not requiring classification for Eye Irrit./Eye Dam. was requested to allow for a substantiated hazard assessment. The registrants concluded based on the available and the recently provided in vitro information (i.e. OECD TG 437) that the substance is damaging to the eye and is to be classified as Eye Dam. 1, H318 (causes serious eye damage). Based on the available data, the eMSCA agrees with this conclusion.

7.9.2.5 Respiratory tract irritation

The registrants concluded that **1,3-dioxolane does not have to be classified for respiratory tract irritation**, and based on the available acute and repeated inhalation toxicity information, the eMSCA agrees with this conclusion. It is noted, however, that no specific information on respiratory tract irritation is available.

7.9.2.6 Skin sensitisation

The registrants concluded that the substance is not sensitising to the skin, and based on the available information (i.e. a reliable negative *in vivo* Local Lymph Node Assay (LLNA) in mice according to OECD TG 429), the eMSCA agrees with this conclusion. Hence, **classification of 1,3-dioxolane for this hazard class is not warranted**.

7.9.3 Repeated dose toxicity

All available reliable repeated dose toxicity studies (Argus Research Laboratories, 1991b; Bio/dynamics, 1981; Toxicology Research Laboratory, 1989; Toxicology Research

Laboratory, 1990) were assessed to derive NOAELs/NOAECs appropriate for risk assessment after prolonged exposure to 1,3-dioxolane.

The major target of 1,3-dioxolane after repeated oral and inhalation exposure of rats is the blood system, i.e. exposure leads to a significant reduction in white blood cell counts. This effect is associated with decreases in the weight of lymphoid organs (such as decreased thymus and spleen weights and/or decreases in bone marrow myeloid cells) and histopathological changes in these organs (e.g. thymic atrophy/oral study, slight reduction in myeloid cells in the bone marrow/inhalation route) in animals of both sexes. These effects may indicate an immunotoxic potential of the substance.

As these effects indicative of direct immunosuppressive effects of the substance are considered relevant for classification only if occurring at concentrations below the guidance values for classification as STOT RE 2 (i.e. at < 1 mg/L/6 h/d in the 90-day study; Table 3.9.2-a in the Guidance on the Application of the CLP criteria), the eMSCA considers that classification of 1,3-dioxolane for STOT RE is not warranted for these effects.

Changes were also observed in the platelet counts of treated animals. While a significant reduction in platelet counts of male and female rats was found after oral substance administration (14 days), a significant increase in platelets counts in both sexes was detected after inhalation exposure (14 days and 90 days). However, the changes in platelet counts were not observed at concentrations relevant for classification for STOT RE.

At higher concentrations exposure further resulted in slight liver toxicity and transient clinical effects, such as decreased alertness and slight incoordination, supporting a narcotic mode of action of the substance (for details see 7.9.2.2). These effects, however, do not justify classification of the substance as STOT RE.

Overall, the eMSCA concludes that available information on repeated dose toxicity **does not justify classification for STOT RE** according to the criteria as laid down in the CLP Regulation.

The following information is considered for DNEL derivation and risk assessment:

7.9.3.1 Oral

The oral $NOAEL_{sys}$ derived for 1,3-dioxolane was 75 mg/kg bw/d for blood effects, based on significantly reduced lymphocyte counts observed in female rats at 250 mg/kg bw/d (= LOAEL) in a reliable 14-d oral repeated dose toxicity study (similar to OECD TG 407 and acc. to GLP; Argus Research Laboratories (1991b)).

7.9.3.2 Inhalation

The $NOAEC_{sys}$ derived for 1,3-dioxolane for blood effects was 0.9 mg/L mainly based on significant reductions in white blood cell and lymphocyte counts and significant increases in platelet counts observed in male and female rats at 3.0 mg/L/6h/d (= LOAEC) in a reliable 90-d inhalation repeated dose toxicity study (similar to OECD TG 413 and acc. to GLP; exposure: 6 h/d, 5 d/week; Toxicology Research Laboratory (1990)).

The sub-acute $NOAEC_{sys}$ was 1.6 mg/L/6 h/d, mainly based on significantly reduced white-blood cell counts and significant increases in platelet counts in male and female rats at the next higher dose, i.e. at 7.0 mg/L/6 h/d (= LOAEC) in a reliable 14-day repeated dose inhalation study in rats (6 /d, 5 d/week, overall 9 exposure treatments; Toxicology Research Laboratory (1989)).

7.9.4 Mutagenicity

Based on negative results of the available and reliable *in vitro* gene mutation studies, i.e. a bacterial reverse mutation assay and a mammalian gene mutation study, and a reliable negative *in vivo* micronucleus assay, it is concluded that there are no indications for 1,3-dioxolane inducing gene mutations or clastogenic/aneugenic effects. Based on the available data which the eMSCA considers sufficient, **classification of 1,3-dioxolane for germ cell mutagenicity is not required** according to the CLP.

7.9.5 Carcinogenicity

There exists a final draft version of a non-guideline, not compliant two-year chronic toxicity study of 1,3-dioxolane in rats with oral substance administration (drinking water at 0.003% and 0.1%). However, a retrospective audit report[11] on this study is available only. In that study no increases in tumour incidences were reported.

Moreover, in the available repeated dose studies performed with 1,3-dioxolane no indications for a carcinogenic potential of 1,3-dioxolane were observed. However, it is noted that (pre-)neoplastic lesions are only rarely documented in (subacute and) sub-chronic repeated dose toxicity studies in general, due to the usually rather long latency of tumour development.

Overall, based on a weight of evidence analysis on the available (limited) data to assess this endpoint **no concern for a carcinogenic potential of 1,3-dioxolane can be derived.**

1,3-Dioxolane may contain formaldehyde in its composition and might be considered a potential formaldehyde releaser. However, the substance is not an intentional formaldehyde releaser, to which regulatory restriction applies. If the formaldehyde concentration in the composition is 0.1 % (for Carc. 1B) or higher (e.g. 1% for Muta. 2), CLP mixture rules would apply for self-classification. This does not apply for the concentrations indicated in the dossiers so far, although some uncertainty on the reporting of the impurities is noted.

7.9.6 Toxicity to reproduction (effects on fertility and developmental toxicity)

7.9.6.1 Effects on fertility and sexual function

Available data (i.e. from repeated dose toxicity studies) are considered insufficient for concluding on fertility effects due to 1,3-dioxolane exposure. An EOGRTS (test method: EU B.56./OECD TG 443) in rats has been requested by ECHA within a dossier evaluation process, as currently no reliable study is available in the registration dossier covering this endpoint according to Annex X of REACH. The study results are expected to become available in 2024, as detailed in the ECHA Dev Decision.[12] The eMSCA is ready to reassess this endpoint upon submission of this additional data.

7.9.6.2 Effects on development

There are two reliable oral PNDT studies available for 1,3-dioxolane (Argus Research Laboratories, 1991a; Charles River Laboratories, 2018). One study was performed with rats and the other one with rabbits. Both studies were performed similar or according to OECD TG 414 and in compliance with GLP.

Overall, given the effects observed in foetuses of rats and rabbits after treatment with 1,3-dioxolane, the eMSCA considers that the evidence is sufficient for classification of 1,3-dioxolane for developmental toxicity, but may not be sufficient for deciding on the appropriate sub-categorisation (i.e. Repr. 1B vs. 2). All adverse foetal developmental effects occurred at maternally toxic dose levels. Moreover, most of the effects observed could be unambiguously interpreted to be variations. Nevertheless, data for variations were above historical control data and malformations (e.g. ventricular septal defects in the heart) have been found at low incidence. Thus, classification criteria of Category 2 seem to be fulfilled, whereas effects may be considered borderline for Category 1B. It is further noted that results from repeated dose toxicity studies with 1,3-dioxolane (e.g. reduced leucocyte and lymphocyte counts in combination with reduction in spleen and thymic weights) raise concern for developmental immunotoxicity. Hence, the eMSCA awaits data from the EOGRTS which was recently requested by ECHA under compliance check in order

[11] https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15807/7/8
[12] https://echa.europa.eu/documents/10162/7f5478d4-256b-22a7-2972-3250029a092c

to decide on the appropriate sub-categorisation and to clarify the developmental immunotoxicity concern from Cohort 3 of the study.

The eMSCA is ready to reassess this endpoint upon submission of this additional data in order to initiate a respective CLH process if considered necessary.

7.9.6.2.1Neurotoxicity

No specific neurotoxicity studies are available for 1,3-dioxolane. Transient and reversible changes in neurobehavioral function consistent with CNS depression were detected in rats after acute and repeated oral and inhalation administration of the substance. Histopathology of the brain was performed in the available and reliable 90-d inhalation study in rats (Toxicology Research Laboratory, 1990). No morphological alterations were reported and evidence on cumulative neurotoxicity was not detected.

The eMSCA concludes that the available data indicate that the observed changes in neurobehavioral functions are due to a narcotic mode of action. Narcotic effects are discussed in section 7.9.2.2.

7.9.7 Hazard assessment of physico-chemical properties

1,3-Dioxolane is classified under the CLP Regulation as flammable liquid in category 2 due to its flashpoint of -5 °C and boiling point of 76 °C. The auto-ignition temperature is 245°C and the lower and upper explosion limit in air were determined to be 2.3 vol% and 30.5 vol%.

In addition, 1,3-dioxolane tends to react with air to form unstable peroxides if it is not inhibited by the addition of an antioxidant.

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

7.9.8.1 Derivation of DNEL(s)

According to section R.8.4 of the REACH Guidance on Information Requirements and Chemical Safety Assessment (ECHA, 2012), a DNEL for the leading health effect needs to be derived for every relevant human population and every relevant route, duration and frequency of exposure, if feasible. The registrants have calculated DNELs which are intended to protect both workers and general population from long-term systemic effects that may be caused after inhalation and dermal exposure to 1,3-dioxolane.

7.9.8.1.1 Overview of typical dose descriptors for all endpoints

The eMSCA calculated the relevant DNELs based on dose descriptors from the available and relevant experimental animal studies. The dose descriptors that were used as Points of Departure (PoDs) are summarised in Table 9. It is noted that the dose descriptor(s) used for DNEL derivation are currently considered provisional only, as results from the EOGRTS requested by ECHA are still pending, which may affect the relevant PoDs and the resulting DNELs.

Table 9

Overview of typical dose descriptors for all relevant endpoints			
Endpoint	**Route**	**Dose descriptor or qualitative effect characterisation; test type**	**Relevant study**
Acute toxicity, specific target organ toxicity after single exposure	oral	**NOAEL: 750 mg/kg bw**; **narcotic effects;** 14 d oral repeated dose toxicity study (rat, reliable; daily administration)	(Argus Research Laboratories, 1991b)

Overview of typical dose descriptors for all relevant endpoints			
Endpoint	**Route**	**Dose descriptor or qualitative effect characterisation; test type**	**Relevant study**
Acute toxicity, specific target organ toxicity after single exposure	dermal	No information available	
Acute toxicity, specific target organ toxicity after single exposure	inhalation	**NOAEC: 7.0 mg/**L **narcotic effects;** 14 d repeated inhalation toxicity study (rat, reliable; exposure: 6 /d, 5 d/week, overall 9 exposure treatments)	(Toxicology Research Laboratory, 1989)
Repeated dose toxicity	oral	**NOAEL: 75 mg/kg bw/day** **Target: blood system; immune system** 14 d oral repeated dose toxicity study (rat, reliable, daily administration)	(Argus Research Laboratories, 1991b)
Repeated dose toxicity	inhalation	***Subchronic:*** **NOAEC: 0.9 mg/L/6h/d** **Target: blood system; immune system** 90 d repeated inhalation toxicity study (rat, reliable; exposure: 6 /d, 5 d/week) ***Subacute:*** **NOAEC: 1.6 mg/L/6h/d** **Target: blood system;** 14 d repeated inhalation toxicity study (rat, reliable; exposure: 6 /d, 5 d/week, overall 9 exposure treatments)	(Toxicology Research Laboratory, 1990) (Toxicology Research Laboratory, 1989)

7.9.8.1.2 DNEL calculation for worker

At the workplace, exposure to 1,3-dioxolane occurs or may occur by inhalation or by dermal contact. Therefore, DNELs have to be derived for both routes of exposure. Since both acute and long-term exposure can be assumed at the workplace, acute and long-term DNELs were calculated. For the DNEL derivation, the eMSCA followed the specifications laid down in REACH Guidance R.8 (ECHA, 2012).

Data from animal experiments in which 1,3-dioxolane was administered orally or via inhalation indicate that exposure to the substance may elicit adverse systemic effects to human health. The blood system is especially affected: Reductions in white blood cell and lymphocyte counts and significant increases in platelet counts in male and female rats were consistently observed in the available studies. A detailed overview of the derivation of the inhalation and dermal DNELs as conducted by the eMSCA is presented in the following tables.

7.9.8.1.2.1 Inhalation

7.9.8.1.2.1.1 Acute DNEL

Table 10

Detailed Overview of the derivation of the $DNEL_{worker, inhalation, acute, narcotic effects}$ for 1,3-dioxolane conducted by the eMSCA		
Description (AF=Assessment factor)	**Value**	**Remark**
Relevant dose descriptor	7.0 mg/L = NOAEC = 7000 mg/m^3	This NOEAC results from a subacute (14 day) inhalation toxicity study in rats (Toxicology Research Laboratory (1989); 6 h/d; 5 d/week). At higher concentrations, transient narcotic effects were observed during/after each treatment.
Modification of the starting point for differences in exposure duration	-	Since the critical endpoint is sedation/narcosis (acute) and the effect was observed every day during/after each treatment, the absolute exposure duration is subordinate. Therefore, the NOAEC is not further adapted.
Modified dose descriptor	7000 mg/m^3	
Overall AFs	**12.5**	
AF for interspecies differences	2.5	A default AF for remaining differences is applied according to REACH Guidance R.8. As explained in section R.8.4.3.1, allometric scaling should not be applied as in cases where doses in experimental animal studies are expressed as concentrations (e.g. in mg/m^3 in air) as these are assumed to be already scaled according to the allometric principle.
AF for intraspecies differences	5	The default factor for workers is applied according to REACH Guidance R.8 because no substance-specific information is available for an adjustment.
AF related to dose response relationship	1	The application of this AF is not necessary because the starting point for the derivation was a NOAEL.
AF related to quality of database	1	The application of this AF is not necessary because the study used is of good quality and reliability.
$DNEL_{worker, inhalation, acute, narcotic effects}$	**560 mg/m^3**	

7.9.8.1.2.1.2 Long-term DNEL

Table 11

Detailed Overview of the derivation of the $DNEL_{worker, inhalation, long term, systemic effects}$ for 1,3-dioxolane conducted by the eMSCA		
Description (AF=Assessment factor)	**Value**	**Remark**
Relevant dose descriptor	0.9 mg/L = NOAEC = 903 mg/m^3	This NOEAC results from a subchronic (90 days) inhalation toxicity study in rats (Toxicology Research Laboratory, 1990). At the dose level of 903 mg/m^3, a statistically significant reduction in white blood cell and lymphocyte counts and increased platelet counts were observed in males and females.
Modification of the starting point	*(6 h/8 h) *(6.7 m^3/10 m^3)	Due to different exposure conditions in the animal experiment and at the workplace of humans both,

Detailed Overview of the derivation of the $DNEL_{worker, inhalation, long term, systemic effects}$ for 1,3-dioxolane conducted by the eMSCA		
Description (AF=Assessment factor)	**Value**	**Remark**
	*(5 d/5 d) *(100%/100%)	time scaling and a modification due to different respiratory volumes have to be applied according to REACH Guidance R.8. The absorption rate for inhalation in rat and in humans was set to 100%, respectively.
Modified dose-descriptor	**453.8 mg/m³**	
Overall AFs	25	
AF for interspecies differences	2.5	A default AF for remaining differences is applied according to the REACH Guidance R.8.
AF for intraspecies differences	5	The default factor for workers is applied according to REACH Guidance R.8 because no substance-specific information is available for further adjustment.
AF for differences in exposure duration	2	This AF was applied according to REACH Guidance R.8 to extrapolate the duration from sub-chronic to chronic.
AF related to dose response relationship	1	As the dose descriptor is a NOAEC already, no AF has to be applied.
AF related to quality of database	1	No AF is applied.
$DNEL_{worker, inhalation, long-term, systemic effects}$	**18.2 mg/m³**	

7.9.8.1.2.2 Dermal Exposure

7.9.8.1.2.2.1 Acute DNEL

Table 12

Detailed Overview of the derivation of the $DNEL_{worker, dermal, acute, narcotic effects}$ for 1,3-dioxolane conducted by the eMSCA		
Description (AF=Assessment factor)	**Value**	**Remark**
Relevant dose descriptor	NOAEL = 750 mg/kg bw/d	This NOAEL for narcotic effects results from a subacute (14 days) oral toxicity study in rats (Argus Research Laboratories, 1991b). At the next higher concentration (2000 mg/kg bw/d), transient narcotic effects were observed after each treatment.
Modification of the starting point	-	Since the critical endpoint is sedation/narcosis (acute) and the effect was observed every day after exposure, the absolute exposure duration is subordinate. Therefore, the NOAEL is not further adjusted. Since substance-specific data is lacking, oral and dermal absorption is considered 100%, no modification for route-to-route extrapolation is applied as well.
Modified dose descriptor	750 mg/kg bw/d	

Detailed Overview of the derivation of the DNEL$_{worker, dermal, acute, narcotic effects}$ for 1,3-dioxolane conducted by the eMSCA		
Description (AF=Assessment factor)	**Value**	**Remark**
Overall AFs	**50**	
AF for interspecies differences - Allometric scaling - remaining differences	 4 2.5	A default AF for allometric scaling and remaining differences is applied according to REACH Guidance R.8.
AF for intraspecies differences	5	The default factor is applied according to REACH Guidance R.8 because no substance-specific information is available for an adjustment.
AF related to dose response relationship	1	The dose descriptor is a NOAEL.
AF related to quality of database	1	No AF is applied.
DNEL$_{worker, dermal, acute, narcotic effects}$	**15 mg/kg bw/d**	

7.9.8.1.2.2.2 Long-term DNEL

Table 13

Detailed Overview of the derivation of the DNEL$_{worker, dermal, long-term, systemic effects}$ for 1,3-dioxolane conducted by the eMSCA		
Description (AF=Assessment factor)	**Value**	**Remark**
Relevant dose descriptor	0.9 mg/L = NOAEC = 903 mg/m^3	This NOEAC results from a subchronic (90 days) inhalation toxicity study in rats (Toxicology Research Laboratory, 1990). At the dose level of 903 mg/m^3 (298 ppm), a statistically significant reduction in white blood cell and lymphocyte counts and increased platelet counts were observed in males and females.
Modification of the starting point	* (0.29 m^3/kg bw/6 h) * (5 d/5 d) * (100%/100%)	Route-to-route extrapolation is needed from inhalation to dermal route. For this purpose the respiratory volume of the rat 0.29 m^3/kg bw for an exposure duration of 6 hours is applied. The absorption rate for inhalation in rat and after dermal exposure in humans was set to 100%, respectively.
Modified dose-descriptor	903 mg/m^3 * 0.29 m^3/kg bw/6 h = **261.9 mg/kg bw/d**	
Overall AFs	100	
AF for interspecies differences - Allometric scaling - remaining differences	 4 2.5	For interspecies differences, default factors for allometric scaling are applied to take into account the difference between the experimental animal and humans and for remaining differences according to REACH Guidance R.8.
AF for intraspecies differences	5	The default factor for workers is applied according to REACH Guidance R.8 because no substance-specific information is available for an adjustment.

Detailed Overview of the derivation of the $DNEL_{worker, dermal, long-term, systemic effects}$ for 1,3-dioxolane conducted by the eMSCA		
Description (AF=Assessment factor)	**Value**	**Remark**
AF for differences in exposure duration	2	This AF was applied according to REACH Guidance R.8 to extrapolate the duration from sub-chronic to chronic.
AF related to dose response relationship	1	As the dose descriptor is a NOAEC already, no AF has to be applied.
AF related to quality of database	1	No AF is applied.
$DNEL_{workers, dermal, long-term, systemic effects}$	**2.6 mg/kg bw/d**	

The DNELs for workers derived by the eMSCA and all further relevant information is summarised in the following table (Table 14).

Table 14

Hazard conclusion for workers - Critical DNELs					
Route	**Type of effect**	**Corrected dose descriptor**	**DNEL**	**Endpoint of concern**	**Critical study**
Inhalation	Acute, narcotic effects	NOAEC = 7000 mg/m^3	560 mg/m^3	Narcotic effects	Toxicology Research Laboratory (1989)
	Long term, systemic effects Effects on blood cells (statistically significant reductions in white blood cell and lymphocyte counts and increased platelet counts in male and female rats)	NOAEC = 453.8 mg/m^3	18.2 mg/m^3	Repeated dose toxicity (by inhalation)	(Toxicology Research Laboratory, 1990)
Dermal	Acute, narcotic effects	NOAEL = 750 mg/kg bw	15 mg/kg bw/d	Narcotic effects	(Argus Research Laboratories, 1991b)
	Long term, systemic effects Effects on blood cells (statistically significant reductions in white blood cell and lymphocyte counts and increased platelet counts in male and female rats)	NOAEL = 261.9 mg/kg bw/d	2.6 mg/ kg bw/d	Repeated dose toxicity (by inhalation)	(Toxicology Research Laboratory, 1990)

7.9.8.1.3 DNEL calculation for consumers and the general population

For the DNEL calculation, the eMSCA followed the specifications given in the REACH Guidance R.8 (ECHA, 2012).

Data from animal experiments, in which 1,3-dioxolane was administered orally or via inhalation, indicate that exposure to the substance may elicit adverse systemic effects to human health. Acute exposure to 1,3-dioxolane leads to transient narcotic effects. After treatment with repeated doses/concentrations of 1,3-dioxolane, blood parameters were affected. More specifically, reductions in white blood cell and lymphocyte counts, significant increases in platelet counts and reduction in spleen weights were observed (see section 7.9.4).

7.9.8.1.3.1 Inhalation

A detailed overview of the derivation of the acute and long-term inhalation DNELs as conducted by the eMSCA is presented in the following tables.

7.9.8.1.3.1.1 Acute DNELs

Table 15

DETAILED OVERVIEW OF THE DERIVATION OF THE DNEL GENERAL POPULATION, INHALATION, ACUTE, NARCOTIC EFFECTS FOR 1,3-DIOXOLANE CONDUCTED BY THE EMSCA		
Description (AF=Assessment factor)	**Value**	**Remark**
Relevant dose descriptor	7.0 mg/L = NOAEC = 7000 mg/m^3	This NOEAC results from a subacute (14 day) inhalation toxicity study in rats (Toxicology Research Laboratory (1989); 6 h/d; 5 d/week). At higher concentrations, transient narcotic effects were observed during/after each treatment.
Modification of the starting point for differences in exposure duration	N/A	Since the critical endpoint is sedation/narcosis (acute) and the effect was observed every day during/after each treatment, the absolute exposure duration is subordinate. Therefore, the NOAEC is not further adjusted.
Modified dose descriptor	$NOAEC_{corr}$ = 7.0 mg/L = 7000 mg/m^3	
Overall AFs	**25**	
AF for interspecies differences	2.5	A default AF for remaining differences (i.e. 2.5) is applied according to the REACH Guidance R.8. According to section R.8.4.3.1, allometric scaling should not be applied in cases where doses in experimental animal studies are expressed as concentrations (e.g. in mg/m³ in air) as these are assumed to be already scaled according to the allometric principle.
AF for intraspecies differences	10	The default factor is applied according to the REACH Guidance R.8 because no substance-specific information is available for an adjustment.
AF related to dose response relationship	1	The dose descriptor is a NOAEC.
AF related to quality of database		No AF is applied.
$DNEL_{general\ population,\ inhalation,\ acute,\ narcotic\ effects}$	**280 mg/m^3**	

7.9.8.1.3.1.2 Long-term DNELs

Table 16

Detailed Overview of the derivation of the DNEL General Population, long-term, inhalation, systemic effects for 1,3-dioxolane conducted by the eMSCA

Description (AF=Assessment factor)	Value	Remark
Relevant dose descriptor	0.9 mg/L = NOAEC = 903 mg/m^3	This NOEAC results from a subchronic (90 day, 6 h/d, 5 d/week) inhalation toxicity study in rats (Toxicology Research Laboratory, 1990). The NOAEC is based on statistically significant reduced white blood cell and lymphocyte counts and increased platelet counts in males and females at the next higher dose (i.e. 3.0 mg/L).
Modification of the starting point	* (5 d/7 d) *(6 h/24 h) * (100 %/100 %)	Due to different exposure conditions in the animal experiment and for the general population time scaling has to be applied according to the REACH Guidance R.8 (24 h/d and 7 d/week). The absorption rate for inhalation in rats and in humans was set to 100 %, respectively.
Modified dose descriptor	**161 mg/m^3**	
Overall AFs	**50**	
AF for interspecies differences - remaining differences	2.5	A default AF for remaining differences (i.e. 2.5) is applied according to the REACH Guidance R.8. According to section R.8.4.3.1, allometric scaling should not be applied in cases where doses in experimental animal studies are expressed as concentrations (e.g., in mg/m³ in air) as these are assumed to be already scaled according to the allometric principle.
AF for intraspecies differences	10	The default factor is applied according to the REACH Guidance R.8 because no substance-specific information is available for an adjustment.
AF for differences in exposure duration	2	This AF was applied according to the REACH Guidance R.8 to extrapolate the duration from sub-chronic to chronic.
AF related to dose response relationship	1	As the dose descriptor is a NOAEC already, no AF has to be applied.
AF related to quality of database	1	Default value.
DNEL$_{\text{general population, inhalation, long-term, systemic effects}}$	**3.2 mg/m^3**	

This DNEL is not identical to but in the same range as the respective DNEL derived by the registrants (i.e. 4.25 mg/m³).

7.9.8.1.3.2 Dermal

A detailed overview of the derivation of the acute and long-term dermal DNELs as conducted by the eMSCA is presented in the following tables.

7.9.8.1.3.2.1 Acute DNELs

Table 17

DETAILED OVERVIEW OF THE DERIVATION OF THE DNEL$_{\text{GENERAL POPULATION, DERMAL, ACUTE, NARCOTIC EFFECTS}}$ FOR 1,3-DIOXOLANE CONDUCTED BY THE EMSCA		
Description (AF=Assessment factor)	**Value**	**Remark**

Relevant dose descriptor	750 mg/kg bw/d = NOAEL	This NOAEL (for narcotic effects) results from a subacute (14 days) oral toxicity study in rats (Argus Research Laboratories, 1991b). At the next higher concentration (i.e. 2000 mg/kg bw/d), transient narcotic effects were observed after each treatment.
Modification of the starting point for differences in exposure duration and route-to-route extrapolation	N/A	Since the critical endpoint is sedation/narcosis (acute) and the effect was observed every day after exposure, the absolute exposure duration is subordinate. Therefore, the NOAEL is not further adjusted. As dermal and oral absorption is considered 100% (substance-specific data is lacking), no modification for route-to-route extrapolation is applied as well.
Modified dose descriptor	NOAEL = 750 mg/kg bw/d	
Overall AFs	**100**	
AF for interspecies differences	10	A default AF for allometric scaling and remaining differences is applied according to the REACH Guidance R.8.
AF for intraspecies differences	10	The default factor is applied according to the REACH Guidance R.8 because no substance-specific information is available for an adjustment.
AF related to dose response relationship	1	The dose descriptor is a NOAEL.
AF related to quality of database		No AF is applied.
$DNEL_{general\ population,\ dermal,\ acute,\ narcotic\ effects}$	**7.5 mg/kg bw/d**	

7.9.8.1.3.2.2 Long-term DNELs

Table 18

DETAILED OVERVIEW OF THE DERIVATION OF THE $DNEL_{GENERAL\ POPULATION,\ LONG-TERM,\ DERMAL,\ SYSTEMIC\ EFFECTS}$ FOR 1,3-DIOXOLANE CONDUCTED BY THE EMSCA		
Description (AF=Assessment factor)	**Value**	**Remark**
Relevant dose descriptor	0.9 mg/L = NOAEC = 903 mg/m^3	This NOEAC results from a subchronic (90 day, 6 h/d, 5 d/week) inhalation toxicity study in rats (Toxicology Research Laboratory, 1990). The NOAEC is based on statistically significant reductions in white blood cell and lymphocyte counts and increased platelet counts in males and females at the next higher dose (i.e. at 3.0 mg/L).
Modification of the starting point	* (5 d/7 d) *(6 h/24 h) * (100 %/100 %) = $NOAEC_{corr}$ = 161 mg/m³ $NOAEC_{corr}$ *1,15 m³/kg bw = $NOAEL_{corr}$ = 185 mg/kg bw/d	Due to different exposure conditions in the animal experiment and for the general population time scaling has to be applied according to the REACH Guidance R.8. The absorption rate for inhalation in rats and after dermal exposure in humans was set to 100 %, respectively. The allometric scaling principle, considering physiological parameter (24 h exposure, 20 m³/person) and including interspecies

		differences (rat/human) and a default bodyweight of the general population (70 kg) according to the REACH Guidance R.8., table R.8-2 is applied for route-to-route extrapolation.
Modified dose-descriptor	**185 mg/kg bw/d**	
Overall AFs	**50**	
AF for interspecies differences - remaining differences	2.5	A default AF for remaining differences (i.e. 2.5) is applied according to the REACH Guidance R.8. The AF for allometric scaling is already included in the factor of 1.15 m³/kg bw for route-to-route extrapolation according to the REACH Guidance R.8.
AF for intraspecies differences	10	The default factor is applied according to the REACH Guidance R.8 because no substance-specific information is available for an adjustment.
AF for differences in exposure duration	2	This AF was applied according to the REACH Guidance R.8 to extrapolate the duration from sub-chronic to chronic.
AF related to dose response relationship	1	As the dose descriptor is a NOAEC already, no AF has to be applied.
AF related to quality of database	1	Default value.
$DNEL_{general\ population,\ dermal,\ long\text{-}term,\ systemic\ effects}$	**3.7 mg/kg bw/d**	

Table 19

DETAILED OVERVIEW OF THE DERIVATION OF THE $DNEL_{GENERAL\ POPULATION,\ DERMAL,\ LONG\text{-}TERM,\ SYSTEMIC\ EFFECTS}$ FOR 1,3-DIOXOLANE CONDUCTED BY THE EMSCA		
Description (AF=Assessment factor)	**Value**	**Remark**
Relevant dose descriptor	75 mg/kg bw/d = NOAEL	This NOAEL (for blood effects) results from a subacute (14 days; daily administration) oral toxicity study in rats (Argus Research Laboratories, 1991b). At the next higher concentration (i.e. 250 mg/kg bw/d), significant reductions in lymphocyte counts were observed.
Modification of the starting point for differences in exposure duration and route-to-route extrapolation	N/A	No AFs for the general population has to be applied for time scaling according to the REACH Guidance R.8, as the substance was administered daily. As dermal and oral absorption is considered 100% (substance-specific data is lacking), no modification for route-to-route extrapolation is applied.
Modified dose-descriptor	NOAEL = 75 mg/kg bw/d	
Overall AFs	**600**	
AF for interspecies differences	10	A default AF for allometric scaling (i.e. 4) and remaining differences (i.e. 2.5) is applied according to the REACH Guidance R.8.

AF for intraspecies differences	10	The default factor is applied according to the REACH Guidance R.8 because no substance-specific information is available for an adjustment.
AF related to exposure duration	6	Default AF for extrapolation from subacute to chronic is applied according to REACH Guidance R.8.
AF related to dose response relationship	1	The dose descriptor is a NOAEL.
AF related to quality of database	1	No AF is applied.
$DNEL_{general\ population,\ dermal,\ acute,\ narcotic\ effects}$	**0.13 mg/kg bw/d**	

The robustness of the long-term DNEL value of 0.13 mg/kg bw/d (24 h/d) based on the NOAEL resulting from a subacute oral study (14 days) is supported by the long-term DNEL of 3.7 mg/m³ that was calculated alternatively using the NOAEC of 0.9 mg/m³ from the subchronic inhalation study in rats as PoD and applying route-to-route-extrapolation, as both lie in a similarly low range.

These DNELs are in the same range as the respective long-term dermal DNEL derived by the registrants (i.e. 1.31 mg/kg bw/d).

Table 20: Hazard conclusions for general population

CRITICAL DNELS					
Route	**Type of effect**	**Corrected dose descriptor**	**DNEL**	**Endpoint of concern**	**Critical study**
Inhalation	Acute, narcotic effects	$NOAEC_{corr}$ = **7000 mg/m³** (for narcotic effects)	**280 mg/m³**	Narcotic effects	(Toxicology Research Laboratory, 1989) Repeated inhalation toxicity study, 14 d
Inhalation	Long-term, systemic effects	$NOAEC_{corr}$ = **161 mg/m³**	**3.2 g/m³**	Effects on the blood system/immune system (statistically significant reductions in white blood cell and lymphocyte counts and increased platelet counts in males and females)	(Toxicology Research Laboratory, 1990) Repeated inhalation toxicity study, 90 d
Dermal	Acute, narcotic effects	$NOAEL_{corr}$ = **750 mg/kg bw**	**7.5 mg/kg bw**	Narcotic effects	(Argus Research Laboratories, 1991b) Oral repeated

					dose toxicity study, 14 d
Dermal	Long-term, systemic effects	$NOAEL_{corr}$ = **185 mg/kg bw/d**	**3.7 mg/kg bw/d**	Effects on the blood system/immune system (statistically significant reductions in white blood cell and lymphocyte counts and increased platelet counts in males and females)	(Toxicology Research Laboratory, 1990) Repeated inhalation toxicity study, 90 d
Dermal	Systemic effects, long-term	$NOAEL_{corr}$ = **75 mg/kg bw/d**	**0.13 mg/kg bw/d**	Effects on the blood system/immune system (statistically significant reductions in white blood cell counts in females)	(Argus Research Laboratories, 1991b) Oral repeated dose toxicity study, 14 d

7.9.9 Conclusions of the human health hazard assessment and related classification and labelling

Based on available and reliable animal data, the eMSCA concludes that classification and labelling of 1,3-dioxolane is not warranted for the hazard classes Acute Toxicity, Skin and Respiratory Irritation, Skin Sensitisation, Specific Target Organ Toxicity – Single Exposure (STOT SE 1 or 2) and Repeated Exposure (STOT RE), Germ Cell Mutagenicity and Carcinogenicity at the present stage of knowledge.

Based on the observed changes of transient nature in neurobehavioural function consistent with CNS depression in the available acute and repeated animal studies and supported by some information found for humans, the eMSCA concludes that **1,3-dioxolane meets the criteria for classification and labelling as STOT SE 3, H336 (May cause drowsiness or dizziness)** for narcotic effects according to CLP (Annex I, Part 3.8.2.2.2). Moreover, based on the results of the recently provided *in vitro* information (i.e. BCOP test according to OECD TG 437), 1,3-dioxolane is damaging to the eyes and has to be classified as **Eye Dam. 1, H318 (Causes serious eye damage).**

In addition, observed effects in foetuses of rats and rabbits after prenatal treatment with 1,3-dioxolane are indicative of **the need for classification of 1,3-dioxolane for developmental toxicity**, but data may not be sufficient for deciding on the appropriate sub-categorisation (i.e. Repr. 1B, H360D vs. Repr. 2, H361d). Classification criteria of Category 2 seem to be fulfilled, whereas effects may be considered borderline for Category 1B. Therefore, data of the EOGRTS which was recently requested by ECHA within a CCH, is awaited in order to decide on the appropriate sub-categorisation for this hazard class and for fertility and sexual function. The eMSCA is ready to reassess the properties of 1,3-dioxolane with regard to reproductive toxicity upon submission of this additional data and may subsequently initiate a respective CLH process if considered necessary. In case the eMSCA will submit a CLH proposal for 1,3-dioxolane, the hazard classes STOT SE 3 (narcotic effects) and Eye Dam. will be addressed as well.

7.10 Assessment of endocrine disrupting (ED) properties

ED properties were not in the scope of the present substance evaluation.

7.11 PBT and VPVB assessment

PBT and vPvB assessment was not in the scope of the present substance evaluation.

7.12 Exposure assessment

7.12.1 Human health

7.12.1.1 Workers

As described in section 7.5.2, 1,3-dioxolane is mainly used in the production of polymers or as a part of polymers (reacted monomer). 1,3-Dioxolane is an intermediate (co-monomer) in the manufacturing process of polyoxymethylene (POM), but it also serves as an aprotic solvent in the manufacturing process of other polymers, as it shows high degrees of solvency also for polar polymers (e.g. polyurethanes, polyesters, epoxies, PVCs). As manufacture of polymers takes place at industrial sites where adequate exposure control measures are supposed to be at place, the exposure situation can be considered adequately controlled for this type of setting and will not be further discussed in this section.

In this worker exposure assessment, focus is laid on exposure scenarios of wide dispersive uses with high potential for human exposure such as, i.e. coatings and paints, thinners, paint removers; lubricants, greases and release products as well as binders and release agents.

The registrants did not supply measurement data on workplace exposure to 1,3-dioxolane and no measurement data was available to the eMSCA for the exposure assessment. In a routine request at the beginning of the SEv process the eMSCA asked the Institute for Occupational Safety and Health of the German Social Accident Insurance (IFA) for information on workplace exposure to 1,3-dioxolane from the MEGA database.[13] The official response from IFA was that there are no entries in the MEGA database for 1,3-dioxolane. This finding can be interpreted in a way that 1,3-dioxolane is not frequently used at German workplaces or, if used, then in such low quantities that it is supposed to be of minor importance. As stated in section 7.5.2, it appears that 1,3-dioxolane is mostly used in specialty products with low market volumes.

During consultations at the beginning of the SEv process, the eMSCA learned from the registrants that of these uses, paint removers/paint strippers are the main application (accounting for roughly 50 % of the total volume sold for uses other than manufacture of polymers). Paint removers/paint strippers mainly consist of solvents and 1,3-dioxolane may as well serve as the main component (up to 100 %) for many formulations based on the substance. The use of 1,3-dioxolane for paint removal by professional workers is also the key scenario for this assessment, which can lead to the highest exposure levels, as the substance can be applied in very high concentrations, even in pure form and in a wide dispersive manner, e.g. brushed, wiped or sprayed on large surfaces. Further scenarios with high potential for worker exposure are widespread use by professional workers in lubricants, greases, release products, in binders and release agents and in anti-freeze and de-icing products. Within these exposure scenarios PROC 10 (roller application or brushing), PROC 11 (non-industrial spraying), and PROC 13 (treatment of articles by dipping and pouring) are those contributing scenarios with the highest potential for human exposure during the application phase of particular relevance.

[13] MEGA is the acronym for "**M**essdaten zur **E**xposition gegenüber **G**efahrstoffen am **A**rbeitsplatz" in German which translates to "Measurement data relating to workplace exposure to hazardous substances". The MEGA exposure database is maintained and evaluated for the institutions for statutory accident insurance and prevention by IFA (Institute for Occupational Safety and Health of the German Social Accident Insurance, "Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung" in Germany). The MEGA database pools workplace exposure measurement data for 871 hazardous chemicals and it can be assumed that most of the hazardous substances with some significance with respect to exposure at workplaces in Germany are covered by the MEGA database.

Exposure estimates for these worker contributing scenarios in the registration dossier(s) (dated March 2021) were generated with the ECETOC TRA worker tool. However, some assumptions that were made in the choice of the input parameters for exposure modelling appear to be overoptimistic and are therefore not justified in the opinion of the eMSCA.

This is in particular the case for assuming that an effective exposure reduction can be guaranteed by the use of local exhaust ventilation (LEV) during the application phases of 1,3-dioxolane (and products containing the substance) in wide dispersive uses by professional workers in particular covered by PROC 10, PROC 11, and PROC 13. For example, it is highly unlikely that a LEV can be effectively installed when professional workers apply paint removers in confined spaces, e.g. to remove coatings from doorframes or stair handles, etc. Such too optimistic choice of model input parameters is also not justified by the use maps developed by downstream user sector organisations under the Exchange Network on Exposure Scenarios (ENES) and published by ECHA.[14]

Therefore, the eMSCA calculated these exposure scenarios using ECETOC TRA (v3.1) according to the input parameters in the registration dossier(s) (dated March 2021), but without considering LEV.

In addition, to obtain conservative estimates, the eMSCA also recalculated the exposure levels for critical exposure situations with ECETOC TRA version 3.1, where possible using the input parameters according to the SWEDs (Sector Specific Workers Exposure Determinants) in the use maps as indicated in the row "model parameter".[15,16]

The results are listed in Table 21.

Table 21

Recalculated exposure levels for the critical contributing scenarios			
Scenario	**Model parameter**	**Long term inhalation exposure estimate**	**Long term dermal exposure estimate**
Widespread use by professional workers, Coatings and Paints, Thinners, Paint removers WCS PROC 10	**Registration:** Professional setting Concentration 5-25% Duration 1-4 hours Indoors Basic ventilation RPE 95% reduction Gloves 80% reduction	9.0 mg/m³	1.97 mg/kg bw/day
	CEPE SWED 68:[15] PROC 10 Professional setting Concentration 100% Duration 8 hours Indoors Good ventilation (3-5 ACH) No RPE Gloves 80% reduction	1079 mg/m³	5.49 mg/kg bw/day
Widespread use by professional workers, Coatings and Paints, Thinners, Paint removers WCS PROC 11	**Registration:** Professional setting Concentration 5-25% Duration <1 hour Indoors Basic ventilation RPE 95% reduction Gloves 80% reduction	6.0 mg/m³	2.57 mg/kg bw/day

[14] https://echa.europa.eu/csr-es-roadmap/use-maps/use-maps-library

[15] https://echa.europa.eu/documents/10162/8718351/cepe_swed_v2_Jan2021_en.xlsx

[16] https://echa.europa.eu/documents/10162/2238308/efcc_swed_v2_en.xlsx

Recalculated exposure levels for the critical contributing scenarios			
Scenario	**Model parameter**	**Long term inhalation exposure estimate**	**Long term dermal exposure estimate**
	CEPE SWED 64:[15] PROC 11 Professional setting Concentration 100 % Duration 8 hours Indoors Good ventilation (3-5 ACH) RPE 90% reduction Gloves 80% reduction	216 mg/m³	21.4 mg/kg bw/day
Widespread use by professional workers; Lubricants, Greases, Release Products WCS PROC 10	Registration: Professional setting Concentration 100 % Duration 1-4 hours Indoors Good ventilation (3-5 ACH) RPE 95 % reduction Gloves 80 % reduction	10.5 mg/m³	3.29 mg/kg bw/day
	EFCC SWED PW_S_li_10_i_II_v2 PROC 10 Professional setting Duration 1-4 hours Indoors Good ventilation (3-5 ACH) No RPE Concentration 100 % Gloves 90 % reduction	648 mg/m³	1.65 mg/kg bw/day
Widespread use by professional workers; Lubricants, Greases, Release Products WCS PROC 11	**Registration:** Professional setting Concentration 100 % Duration <1 hour Indoors Basic ventilation RPE 95 % reduction Gloves 80 % reduction	6.0 mg/m³	2.57 mg/kg bw/day
	EFCC SWED PW_li_11_i_III_v2 PROC 11 Professional setting Duration <1 hour Indoors Basic ventilation RPE 90 % reduction Concentration <25 % Gloves 90 % reduction	37 mg/m³	1.29 mg/kg bw/day
Widespread use by professional workers; Lubricants, Greases, Release Products WCS PROC 13	**Registration:** Professional setting Concentration 100 % Duration 8 hours Indoors Basic ventilation RPE 95 % reduction Gloves 80 % reduction	12.5 mg/m³	2.74 mg/kg bw/day

Recalculated exposure levels for the critical contributing scenarios			
Scenario	**Model parameter**	**Long term inhalation exposure estimate**	**Long term dermal exposure estimate**
	EFCC SWED PW_S_li_13_i_II_v2 PROC 13 Professional setting Duration 8 hours Indoors Good ventilation (3-5 ACH) No RPE Concentration 100 % Gloves 90 % reduction	540 mg/m³	1.37 mg/kg bw/day
Widespread use by professional workers; Binders and release agents WCS PROC 10	**Registration:** Professional setting Concentration 5-25 % Duration 1-4 hours Indoors Good ventilation (3-5 ACH) RPE 90 % reduction Gloves 80 % reduction	12.6 mg/m³	1.97 mg/kg bw/day
	EFCC SWED PW_S_li_10_i_III_v2 PROC 10 Professional setting Duration 1-4 hours Indoors Good ventilation (3-5 ACH) No RPE Concentration 100 % Gloves 90 % reduction	648 mg/m³	1.65 mg/kg bw/day
Widespread use by professional workers; Binders and release agents WCS PROC 11	**Registration:** Professional setting Concentration 5-25 % Duration <1 hour Indoors Basic ventilation RPE 90 % reduction Gloves 80 % reduction	12.0 mg/m³	2.57 mg/kg bw/day
	EFCC SWED PW_li_11_i_III_v2 PROC 11 Professional setting Duration 1-4 hours Indoors Basic ventilation RPE 90 % reduction Concentration <25 % Gloves 90 % reduction	111 mg/m³	3.86 mg/kg bw/day

7.12.1.2 Consumers

The initial grounds for concern were the following: Use of high product amounts in combination with high concentrations of volatile solvents in consumer products – (e.g. DIY products PC 1 & PC 9a) can lead to high exposure.

Most of the registrants do not report any consumer uses in their dossier(s). Others carried out a downstream user surveys and internet searches. New data regarding consumer exposure and risk characterisation were provided during the evaluation period.

1,3-Dioxolane is used as a solvent in several consumer products. According to the information provided on the dissemination website within “Chemical Substance Search” (on 2016-11-28, status: last updated: 31/08/2016) several product categories are listed

for coatings, cleaning agents, lubricants, and cosmetics (see above). These uses are in line with the findings of secondary sources: consultation of product data bases of Germany, Slovenia, Switzerland, and the Nordic Countries (SPIN), as well as researching safety data sheets.

1,3-Dioxolane is an ingredient in cleaning agents for specific purposes like removing oil and grease stains from barbecues, deep frying pans, or other surfaces. It is also used in glue removers and as an alternative for dichloromethane in paint strippers. Several formulations are reported with 1,3-dioxolane concentrations up to 86 % (Zarogiannis et al., 2007).

The use of such consumer products could lead to exposure predominantly by inhalation and dermal contact. Due to a vapour pressure of 10 100 Pa (20 °C), special attention was paid to inhalation exposure.

At the beginning of the Substance Evaluation in March 2016 registrants with consumer uses have submitted an update of their CSR. In this updated CSR, some of the consumer uses have been removed (PC 3, 4, 9b, 9c, 18, 29, 31, 38) while others have been adapted, e.g. by heavily reducing the concentration of 1,3-dioxolane in the exposure scenarios. In consequence, substance concentrations in the exposure scenarios are not consistent with the much higher concentrations as reported in some SDS and are not in line with the reported technical function of 1,3-dioxolane as a solvent. However, consumer uses which gave cause of concern regarding sensitive population (in particular children) are no longer supported by registrants. Furthermore, the use in PC 9b (fillers, putties, plasters, modelling clay) and PC 9c (finger paints) are advised against.

It was not possible to conclusively clarify, neither in dialogue with the registrants nor through their informal dossier update during the evaluation year, what is practically done with the substance in the market. Therefore, the concerns identified regarding consumer exposure could not be elucidated. Hence, there is a need for better understanding of the consumer market with its diversity of applications to finally assess exposure to 1,3-dioxolane. In this regard, the ongoing RMOA (for details see the respective RMOA section on ECHA's website)[17] is considered essential for obtaining a better understanding of the variety of consumer products on the market using solvents such as 1,3-dioxolane and to enable an exposure estimation and risk assessment.

7.12.2 Environment

Not in scope of the present substance evaluation.

7.13 Risk characterisation

7.13.1 Worker

Considering the physicochemical properties of 1,3-dioxolane and its industrial and professional uses, workplace exposure occurs mainly via inhalation and dermal contact. For quantitative risk characterisation of 1,3-dioxolane, dermal and inhalation exposure estimates were compared with the derived long-term systemic dermal and inhalation DNELs, respectively. The obtained risk characterisation ratios (RCR) were then added up to calculate the combined RCRs for each exposure scenario.

For 1,3-dioxolane, long term systemic DNELs for inhalation of 18.2 mg/m^3 and for dermal contact of 2.6 mg/kg bw/day were derived. The DNEL values were calculated on the basis of a sub-chronic inhalation study in rats (Toxicology Research Laboratory, 1990). A detailed overview of how the eMSCA derived these DNELs is given in section 7.9.9.

[17] RMOA of the DE CA on several solvents, among them 1,3-dioxolane: https://echa.europa.eu/de/assessment-regulatory-needs/-/dislist/details/0b0236e184ff4c72

For uses of 1,3-dioxolane at industrial sites, exposure is supposed to be adequately controlled. For this reason, risk characterisation is focused on the critical exposure scenarios as described above (7.12.1.1), which are covering the application phases of the substance/products, in particular PROC 10 (roller application or brushing), PROC 11 (non-industrial spraying), and PROC 13 (treatment of articles by dipping and pouring).

An overview of the RCRs calculated by the eMSCA with the derived DNELs (workers, inhalation or dermal route, systemic, long term) is given in Table 22.

Note: For the risk assessment of the professional worker, the acute DNELs are an important information but they were not used for the risk assessment, since short term exposures within a scenario (e.g. mixing and loading) are considered to be covered by the long term exposure estimates (e.g. for the application phase), especially as the values for the acute DNELs for the inhalation and dermal routes are much higher than those for the long-term DNELs.

Table 22: Overview of RCRs calculated by the eMSCA in critical exposure scenarios

Exposure scenario	Modelling parameter rationale	Highest predicted exposure value per route		RCR per route		Total RCR
		Inhalation (mg/m³)	Dermal (mg/kg bw/d)	Inhalation	Dermal	= RCR Inhalation + RCR dermal
Widespread use by professional workers, Coatings and Paints, Thinners, Paint removers WCS PROC 10	CSR without LEV	9.0	1.97	0.49	0.76	**1.25**
	SWED	1079	5.49	59.3	2.1	61.4
Widespread use by professional workers, Coatings and Paints, Thinners, Paint removers WCS PROC 11	CSR without LEV	6.0	2.57	0.33	**0.99**	**1.32**
	SWED	216	21.4	11.9	8.2	20.1
Widespread use by professional workers; Lubricants, Greases, Release Products WCS PROC 10	CSR without LEV	10.5	3.29	0.58	**1.27**	**1.85**
	SWED	648	1.65	35.6	0.6	36.2
Widespread use by professional workers; Lubricants, Greases, Release Products WCS PROC 11	CSR without LEV	6.0	2.57	0.33	**0.99**	**1.3**
	SWED	37	1.29	2	0.5	2.5

Exposure scenario	Modelling parameter rationale	Highest predicted exposure value per route		RCR per route		Total RCR
		Inhalation (mg/m³)	Dermal (mg/kg bw/d)	Inhalation	Dermal	= RCR Inhalation + RCR dermal
Widespread use by professional workers; Lubricants, Greases, Release Products WCS PROC 13	CSR without LEV	12.5	2.74	0.69	**1.15**	**1.8**
	SWED	540	1.37	29.7	0.53	29.5
Widespread use by professional workers; Binders and release agents WCS PROC 10	CSR without LEV	12.6	1.97	0.69	0.76	**1.5**
	SWED	648	1.65	35.6	0.63	36.2
Widespread use by professional workers; Binders and release agents WCS PROC 11	CSR without LEV	12.0	2.57	0.66	**0.99**	**1.65**
	SWED	111	3.86	6.1	1.49	7.6

7.13.1.1 Risk assessment using exposure data from CSR without LEV

For the further discussion of the risk characterisation, only the RCRs calculated from exposure values based on the parameters provided in the registration dossier(s) are considered, but without taking LEV into account.

The RCRs calculated from the SWED input parameters exceed the values obtained based on the use conditions specified by the registrant(s) (disregarding LEV). However, while the input parameters used by the registrant(s) are considered too optimistic by the eMSCA, the input parameters according to SWED, and hence the RCRs calculated from them, might be too conservative (as they are not fully representative for the actual use conditions). Therefore, these values are shown for comparison, only, and are not further considered in the discussion of the risk characterisation.

As shown in table 22 the calculated RCRs for exposure by inhalation with values of 0.33 to 0.69 are below 1 and are thus considered acceptable.

For dermal exposure, the RCRs for three uses and five contributing exposure scenarios are below 1 with values ranging from 0.76 to 0.99 and are thus considered acceptable. For 3 of the 7 scenarios, the RCRs are very slightly below 1. Even if the values were only slightly below 1, they still do not represent a risk concern for the worker.

For two exposure scenarios the RCRs were slightly higher than 1 and therefore a risk for the professional user cannot be excluded: for “Lubricants, Grease, Release of products PROC 13” the RCR is 1.15 and for “Lubricants, Grease, Release of products PROC 10” the RCR is 1.27.

The values of the combined RCRs range from 1.25 to 1.8 and the respective uses are thus considered to lead to a risk for the professional user.

In the opinion of the eMSCA, the registrants should consider the newly calculated DNELs (worker, inhalation or dermal route, systemic, long term) and refine the exposure assessment for the purpose of the risk evaluation and communication.

7.13.1.2 Conclusion of the risk characterisation for workers

A final decision about whether these results indicate the need for regulatory action (e.g. restriction) will be made once all relevant information including the pending EOGRTS is available to the eMSCA.

7.13.2 Consumers

For consumers, a comprehensive risk characterisation for 1,3-dioxolane will be included in the follow-up RMOA. Oral exposure of consumers to 1,3-dioxolane was not considered by the eMSCA, while dermal and inhalation exposure of consumers are considered relevant.

It is noted that considerable uncertainties arise specifically when trying to adequately calculate the exposure scenarios (e.g. actual and realistic concentrations of 1,3-dioxolane in the respective products). These uncertainties are addressed in the ongoing RMOA,[17] which was initiated by the eMSCA in 2020 and in which further information on consumer products will be obtained via various sources to improve estimates on consumer exposure and to allow a sound deliberation on the most appropriate regulatory measure(s). After this in-depth evaluation, it will be possible to evaluate whether and for which product categories 1,3-dioxolane poses a human health risk, whether further risk management measures are necessary for its use in consumer products, and, if so, which measure(s) will be considered best suited in order to minimise this risk for consumers.

7.14 References

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7.15 Abbreviations

[sic] *"intentionally so written"*
ACH ..... *Air Changes per Hour*
AF ..... *Assessment Factor*
BCOP ..... *Bovine Corneal Opacity and Permeability*
CCH ..... *Compliance Check*
CEPE ..... *European Council of the Paint, Printing Ink and Artists' Colours*
CLH ..... *Harmonised Classification and Labelling*
CNS ..... *Central Nervous System*
CoRAP ..... *Community Rolling Action Plan*
CSR ..... *Chemical Safety Report*
DE CA ..... *German Competent Authority*
DEv ..... *Dossier Evaluation*
DIY ..... *Do It Yourself (products)*
DNEL ..... *Derived No-Effect Level*
ECETOC ..... *Europan Centre for Ecotxicology and Toxicology of Chemicals*
ECHA ..... *European Chemical Agency*
EFCC ..... *European Federation for Construction Chemicals*
eMSCA ..... *evaluating Member State Competent Authority*
ENES ..... *Exchange Network on Exposure Scenarios*
EOGRTS ..... *Extended One Generation Reproductive Toxicity Study*
ERC ..... *Environmental Release Category*
GLP ..... *Good Laboratory Practice*
HPV ..... *Hight Production Volume Callenge Program*
IFA *Institute for Occupational Safety and Health of the German Social Accident Insurance*
LEV ..... *Local Exhaust Ventilation*, *Local Exhaust Ventilation*
LOAEC ..... *Lowest Observed Adverse Effect Level*
MAK ..... *Maximum Concentration of a Chemical Substance in the Workplace*
MEGA database ..... *Messdaten zur Exposition gegenüber Gefahrstoffen am Arbeitsplatz*
NOAEC ..... *No Observed Adverse Effect Concentration*
NOAEL ..... *No Observed Adverse Effect Level*
OECD ..... *Organisation for Economic Co-operation and Development*
PBT ..... *Persistent, Bioaccumulative and Toxic*
PC ..... *Chemical Product Category*
PNDT ..... *Pre-Natal Development Toxicity*
PoD ..... *Point of Departure*
POM ..... *Polyoxymethylene*
PROC ..... *Process Category*
RCR ..... *Risk Characterisation Ratios*
RMOA ..... *Regulatory Management Option Analysis*
RPE ..... *Rating of Perceived Exertion*
SDS ..... *Safety Data Sheets*
SEv ..... *Substance Evaluation*
STOT RE ..... *Specific Target Organ Toxicity Repeated Exposure*
STOT SE ..... *Specific Target Organ Toxicity Single Exposure*
SVHC ..... *Substance of Very High Concern*
SWED *Sector Specific Workers Exposure Descriptions*, *Sector Specific Workers Exposure Determinants*
Tbd ..... *To be defined*
TRA ..... *Target Risk Assessment*
US EPA ..... *United States Environmental Protection Agency*
vPvB ..... *very Persistent and very Bioaccumulative*
WCS ..... *Worker Contributing Scenario*