

## Annex XV report

# PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE OF VERY HIGH CONCERN ON THE BASIS OF THE CRITERIA SET OUT IN REACH ARTICLE 57

Substance Name: bis(2-(2-methoxyethoxy)ethyl) ether; (tetraglyme)

EC Number: 205-594-7

CAS Number: 143-24-8

Submitted by: Austria

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## ABBREVIATIONS

AC	Article category
C&L	Classification & Labelling
EAA	Ethoxyacetic acid
EGEE	2-ethoxyethanol
EGME	2-methoxyethanol
ERC	Environmental release category
MAA	Methoxyacetic acid
OSPA	Oxygen Solvents Producers Association
PC	Product categories
PROC	Process categories
RAC	Risk Assessment Committee
SVHC	Substance of very high concern
SU	Sector of use

## PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE OF VERY HIGH CONCERN ON THE BASIS OF THE CRITERIA SET OUT IN REACH ARTICLE 57

Substance Name: bis(2-(2-methoxyethoxy)ethyl) ether;  
(tetraglyme)

EC Number: 205-594-7

CAS number: 143-24-8

- The substance is proposed to be identified as a substance meeting the criteria of Article 57 (c) of Regulation (EC) No 1907/2006 (REACH) owing to its classification in the hazard class toxic for reproduction category 1B, H360FD (May damage fertility. May damage the unborn child)<sup>1</sup>.

Summary of how the substance meets the criteria set out in Article 57 of the REACH Regulation

Bis(2-(2-methoxyethoxy)ethyl) ether, referred to hereinafter as tetraglyme, is covered by index number 603-238-00-9 of Regulation (EC) No 1272/2008 in Annex VI, part 3, Table 3.1 (the list of harmonised classification and labelling of hazardous substances) and it is classified in the hazard class toxic for reproduction category 1B (H360FD: May damage fertility. May damage the unborn child).

Therefore, this classification of the substance in Regulation (EC) No 1272/2008 shows that it meets the criteria for classification in the hazard class:

- Toxic for reproduction category 1B (H360FD: May damage fertility. May damage the unborn child) in accordance with Article 57 (c) of the REACH Regulation.

Registration dossiers submitted for the substance? Yes

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<sup>1</sup> Classification in accordance with section 3.7 of Annex I to Regulation (EC) No 1272/2008

## PART I

### Justification

#### Identity of the substance and physical and chemical properties

##### 1.1 Name and other identifiers of the substance

Table 1: Substance identity

EC number:	205-594-7
EC name:	bis(2-(2-methoxyethoxy)ethyl) ether
CAS number (in the EC inventory):	143-24-8
CAS number: Deleted CAS numbers:	Deleted: 70992-84-6
CAS name:	2,5,8,11,14-pentaoxapentadecane
IUPAC name:	2,5,8,11,14-pentaoxapentadecane
Index number in Annex VI of the CLP Regulation	603-238-00-9
Molecular formula:	C <sub>10</sub> H <sub>22</sub> O <sub>5</sub>
Molecular weight range:	222.2787
Synonyms:	Tetraglyme Tetraethylene glycol dimethyl ether TetraEGDME

Bis(2-(2-methoxyethoxy)ethyl) ether equates to the common name tetraglyme, which is used throughout the document.

Structural formula<sup>2</sup>:



<sup>2</sup> Source: European Chemicals Agency, <https://echa.europa.eu/de/substance-information/-/substanceinfo/100.005.086> (accessed 08/2020)

## 1.2 Composition of the substance

Name: bis(2-(2-methoxyethoxy)ethyl) ether; (tetraglyme)

Description: liquid, colourless

Substance type: mono-constituent

The substance is registered as pure substance and as technical grade.

Impurities and/or additives are not relevant for SVHC identification of the substance.

## 1.3 Identity and composition of degradation products/metabolites relevant for the SVHC assessment

Not relevant for the identification of the substance as SVHC in accordance with Article 57 (c) REACH.

## 1.4 Identity and composition of structurally related substances (used in a grouping or read-across approach)

Not relevant for the identification of the substance as SVHC in accordance with Article 57 (c) REACH.

## 1.5 Physicochemical properties

Not relevant for the identification of the substance as SVHC in accordance with Article 57 (c) REACH.

## 2. Harmonised classification and labelling

Bis(2-(2-methoxyethoxy)ethyl) ether; (tetraglyme) is covered by Index number 603-238-00-9 in part 3 of Annex VI to the CLP Regulation as follows:

Table 2: Classification according to draft Annex VI, Table 3.1 (list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008

Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Spec. Conc. Limits, M-factors	Notes
				Hazard Class and Category Code(s)	Hazard statement code(s)	Pictogram, Signal Word Code(s)	Hazard statement code(s)	Suppl. Hazard statement code(s)		
603-238-00-9	bis(2-(2-methoxyethoxy)ethyl) ether, tetraglyme	205-594-7	143-24-8	Repr. 1B	H360FD	GHS08 Dgr	H360FD	-	-	-

## 3. Environmental fate properties

Not relevant for the identification of the substance as SVHC in accordance with Article 57 (c) REACH.

## 4. Human health hazard assessment

Please see Chapter 2 Harmonised Classification and Labelling.

## 5. Environmental hazard assessment

Not relevant for the identification of the substance as SVHC in accordance with Article 57 (c) REACH.

## 6. Conclusions on the SVHC Properties

### 6.1 CMR assessment

Bis(2-(2-methoxyethoxy)ethyl) ether; (tetraglyme) is covered by index number 603-238-00-9 of Regulation (EC) No 1272/2008 in Annex VI, part 3, Table 3.1 (the list of harmonised classification and labelling of hazardous substances) and it is classified in the hazard class toxic for reproduction category 1B (H360FD: May damage fertility. May damage the unborn child).

Therefore, this classification of the substance in Regulation (EC) No 1272/2008 shows that it meets the criteria for classification in the hazard class:

- Toxic for reproduction category 1B (H360FD: May damage fertility. May damage the unborn child) in accordance with Article 57 (c) of the REACH Regulation.

### 6.2 PBT and vPvB assessment

Not relevant for the identification of the substance as SVHC in accordance with Article 57 (c) REACH.

### 6.3 Assessment under Article 57(f)

Not relevant for the identification of the substance as SVHC in accordance with Article 57 (c) REACH.



## Part II

### 7. Registration and C&L notification status

#### 7.1 Registration status

Table 3: Registration status

From the ECHA dissemination site <sup>3</sup>	
Registrations	<input checked="" type="checkbox"/> Full registration(s) (Art. 10)  <input type="checkbox"/> Intermediate registration(s) (Art. 17 and/or 18)

#### 7.2 CLP notification status

Table 4: CLP notifications

	CLP Notifications <sup>4</sup>
Number of aggregated notifications	9
Total number of notifiers	560

### 8. Total tonnage of the substance

Table 5: Tonnage status

Total tonnage band for the registered substance (excluding the volume registered under Art 17 or Art 18) <sup>5</sup>	100+ t/pa
Tonnage information from public sources other than registration dossiers (if available)	-

<sup>3</sup> <https://echa.europa.eu/de/substance-information/-/substanceinfo/100.005.086> (accessed 08/2020)

<sup>4</sup> C&L Inventory database, <http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database> (accessed 08/2020)

<sup>5</sup> <https://echa.europa.eu/de/substance-information/-/substanceinfo/100.005.086> (accessed 08/2020)

## 9. Information on uses of the substance

Table 6: Uses (according ECHA dissemination site; 10/06/2020)

	Use(s)	Registered use	Use likely to be in the scope of Authorisation
Manufacture	Manufacture of the substance <i>PROC 1, 3, 4, 8b, 15</i>	Yes	Yes
Uses as intermediate	-	No	No
Formulation or repacking	Formulation of preparations <i>PROC 1, 2, 3, 5; ERC2: Formulation into mixture</i> Formulation of preparations, professional <i>PROC 3, 5; ERC2: Formulation into mixture</i> Solder Flux <i>PROC 5, 14; ERC3: Formulation into solid matrix; PC 38: Welding and soldering products, flux products</i>	Yes	Yes
Uses at industrial sites	Agent absorbing gases <i>PROC 2; ERC7: Use of functional fluid at industrial site, PC 0: Other: agent absorbing gases, SU 0: Other: industrial manufacturing</i> Industrial use of tetraglyme as gas absorption liquid <i>PROC 1, 2, 3, 8b, 15; ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article), PC 40: Extraction agents, SU 0: Other, SU3: Industrial uses: Uses of substances as such or in preparations at industrial sites</i> Use in industrial chemical processes <i>PROC 1, 2, 3; ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article); ERC7: Use of functional fluid at industrial site, SU 0: Other, SU 3 Industrial Manufacturing (all)</i> Industrial use of tetraglyme as	Yes	Yes

	<p>solvent in synthesis reactions or as extracting agent</p> <p><i>PROC 1, 2, 3, 8b, 15; ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article), PC 0: solvent; SU 8: Manufacture of bulk, large scale chemicals, SU 9: Manufacture of fine chemicals, SU 3: industrial use – uses of substances as such or in preparations at industrial sites</i></p> <p>Solvent</p> <p><i>PROC 3, 8b; ERC6a: Use of intermediate; PC 27: Plant protection products, SU 9: Manufacture of fine chemicals</i></p> <p>Use in functional fluids</p> <p><i>PROC 17, 18; ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article), SU 3 Industrial Manufacturing</i></p> <p>Charging and discharging of substances and mixtures</p> <p><i>PROC 8a, 8b, 9; ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article), SU 0: Other: SU 3 Industrial Manufacturing (all)</i></p> <p>Use in laboratories</p> <p><i>PROC 15; ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article), SU 0: Other: SU 3 Industrial Manufacturing (all)</i></p> <p>Industrial use</p> <p><i>PROC 1, 2, 3, 8b, 15; ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article); PC 0: solvent, SU 8: Manufacture of bulk, large scale chemicals (including petroleum products), SU 9: Manufacture of fine chemicals, SU 0: Other, SU 3: Industrial uses: Uses of substances as such or in preparations at industrial sites</i></p> <p>Waste (Hazardous waste incineration)</p> <p><i>ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article); PC 27: Plant protection products</i></p>		
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<p>Uses by professional workers</p>	<p>Use in Functional Fluids, professional <i>PROC 17, 18, 20; ERC8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor)</i></p> <p>Use in laboratories, professional <i>PROC 15; ERC8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor)</i></p> <p>Charging and discharging of substances and mixtures, professional <i>PROC 8a, 8b, 9; ERC8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor)</i></p> <p>Use of ink by professionals <i>PROC 1; ERC8c: Widespread use leading to inclusion into/onto article (indoor); PC 18 Ink and toners, SU 7: Printing and reproduction of recorded media</i></p>	<p>Yes</p>	<p>Yes</p>
<p>Consumer uses</p>	<p>Not recommended for use in any consumer products (use advised against)</p>	<p>No</p>	<p>No</p>
<p>Article service life</p>	<p>Service life of printed paper articles <i>AC8: Paper articles, ERC11a: Widespread use of articles with low release (indoor)</i></p>	<p>Yes</p>	<p>No</p>

- PROC 1: Chemical production or refinery in closed process without likelihood of exposure or processes with equivalent containment conditions
- PROC 2: Chemical production or refinery in closed continuous process with occasional controlled exposure or processes with equivalent containment conditions
- PROC 3: Manufacture or formulation in the chemical industry in closed batch processes with occasional controlled exposure or processes with equivalent containment conditions
- PROC 4: Chemical production where opportunity for exposure arises
- PROC 5: Mixing or blending in batch processes
- PROC 8a: Transfer of substance or mixture (charging and discharging) at non-dedicated facilities
- PROC 8b: Transfer of substance or mixture (charging and discharging) at dedicated facilities
- PROC 9: Transfer of substance or mixture into small containers (dedicated filling line, including weighing)
- PROC 14: Tableting, compression, extrusion, pelletisation, granulation
- PROC 15: Use as laboratory reagent
- PROC 17: Lubrication at high energy conditions in metal working operations
- PROC 18: General greasing / lubrication at high kinetic energy conditions
- PROC 20: Use of functional fluids in small devices

Tetraglyme belongs to the group of glycol ethers, which in general have very good solvent properties. Tang and Zhao (2014) investigated the use of glymes (glycol diethers) and mentioned the high boiling point (275°C), high stability and high solubility of inorganic salts as the solvent features of tetraglyme. The substance is a strong chelating agent for Na<sup>+</sup> ions and is suitable for reactions at low temperatures due to a low freezing point (-30°C). The author listed the following industrial applications for tetraglyme: Flue gas cleaning systems, solvent for production of binders for paints, coalescing agent in paint formulations, adhesives production, electrodeposition, manufacture of soldering fluxes/solder pastes,

adsorption liquid and gas scrubbing, formulations of paint strippers and adhesive removers, extraction of volatile organic compounds from solid wastes, inert additive for the fixation of methylated methylolmelamine resins in durable-press cotton and cellulosic fabrics, an HFC/CFC lubricant (automotive air conditioning (A/C) compressor).

The substance can also be used in lithium-ion battery technology and in the selective adsorption of proteins during the promotion of cell adhesion<sup>6</sup>. According to BASF the specific function of tetraglyme in inks is as emulsifier to stabilise inks and to function as humectant to keep orifices clear<sup>7</sup>.

The SPIN database<sup>8</sup> includes the following use descriptions with low amounts for tetraglyme in the years 2016/17: printing and reproduction of recorded media, manufacture of computer, electronic and optical products. Use categories are colouring agent, reprographic agent and lubricants/additives. Use in consumer preparations has been indicated by Sweden for 2017.

The European producers of glycol ethers (members of OSPA), set up a charter<sup>9</sup> (in 1996) where commitments and actions that are being undertaken to avoid the risks linked to glycol ethers classified toxic for reproduction are stated. The charter forbids, under penalty of non-delivery, all uses of glycol ethers classified as reprotoxic in any product sold to the public and strictly limits the use of glycol ethers classified toxic for reproduction category 1B to industrial applications, for which no substitute has been found so far. All customers must ensure that occupational exposures/emissions are within the legal constraints and that there is no remaining residue of these glycol ethers left in the end product. The charter must be signed by buyers (from direct customers) as well as by any distributor involved. The producers oblige all buyers to annually reconfirm the application of the charter.

According to information on their website<sup>10</sup> OSPA members pay particular attention to promoting alternatives to glycol ethers classified as "Toxic for reproduction".

## 10. Information on structure of the supply chain

According to ECHA's dissemination site (brief profile<sup>11</sup>, accessed 06/2020) tetraglyme has six active registrations under REACH, one joint submission and no individual submissions. The REACH registrants are located in six different member states indicating a medium distribution across the EU.

A high number of C&L notifications (496, 9 aggregated notifications) is reported on ECHA's dissemination site.

The substance is registered for manufacture, formulation, use at industrial sites, use by professionals and article service life. Consumer use is not registered, however, information in the SPIN database indicates use in consumer preparations. The technical functions, as given in the registration dossiers are as solvent and as

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<sup>6</sup> <https://www.alfa.com/de/catalog/020443/>

<sup>7</sup> [http://www.intermediates.basf.com/chemicals/web/en/function/conversions:/publish/content/news-and-publications/brochures/download/BASF\\_Brochure\\_High-Performance-Solvents.pdf](http://www.intermediates.basf.com/chemicals/web/en/function/conversions:/publish/content/news-and-publications/brochures/download/BASF_Brochure_High-Performance-Solvents.pdf)

<sup>8</sup> Substances in Preparations in the Nordic countries <https://eng.mst.dk/chemicals/chemicals-in-products/assessment-of-chemicals/spin-database/>

<sup>9</sup> <https://www.glycol-ethers.eu/glycol-ethers-charter/>

<sup>10</sup> <https://www.glycol-ethers.eu/a-responsible-industry/>

<sup>11</sup> <https://echa.europa.eu/de/brief-profile/-/briefprofile/100.005.086>

agent adsorbing and absorbing gases or liquids, which overall indicates a limited diversity of uses.

According to public registration information<sup>12</sup>, tetraglyme has diverse actors (manufacture, formulation, use at industrial sites and by professionals, article service life) and is used in five product categories, five sectors of use and one article category (see Table 6).

No information is available on the number of industrial sites. A medium to high complexity of the supply chain is assumed.

## 11. Additional information

### 11.1 Substances with similar hazard and use profiles on the Candidate List

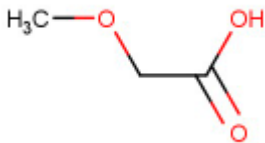
Tetraglyme belongs to a group of ethylene glycol ethers where all members, based on their chemical structure may lead to the formation of the metabolites methoxyacetic acid (MAA) and/or 2-methoxyethanol (EGME) in the body. MAA and EGME have been identified as the likely active metabolites associated with reproductive toxicity effects of the short-chain glycol ethers belonging to this group. This was also considered by RAC in its opinion on the harmonised classification of tetraglyme. Similar substances and metabolites are presented in Table 7 below (substances 1-5).

Other short-chain ethylene glycol ethers lead to the formation of the metabolites ethoxyacetic acid (EAA) or 2-ethoxyethanol (EGEE) in the body. EAA tends to be cleared at a faster rate than MAA in smaller organisms but is of concern due to its reproductive toxicity, too (Table 7, substances 6-8).

Out of these groups of similar glycol ethers described above, all eight substances have been identified as SVHCs in the years 2010 - 2012 due to their reproductive toxicity effects (Repr. 1B). Diglyme has already been included in Annex XIV, REACH.

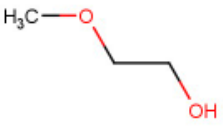



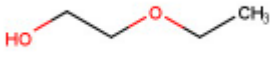
Ethylene glycol ethers are used as solvents or functional fluids. Given the structural similarity of these substances, the same technical functions and the overlap between uses within this group, substitution between them seems highly likely (for more information see Chapter 11.2). Tetraglyme might serve as alternative to already regulated low molecular weight glymes.

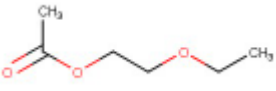

Table 7: Similar substances and metabolites and their regulatory status.

No	Substance identity	Chemical structure  (source: European Chemicals Agency, <a href="http://echa.europa.eu/">http://echa.europa.eu/</a> )	Regulatory status
1	Methoxyacetic acid,  MAA  EC 210-894-6		Candidate list

<sup>12</sup> ECHA dissemination site <https://echa.europa.eu/de/registration-dossier/-/registered-dossier/14547>

ANNEX XV – IDENTIFICATION OF BIS(2-(2-METHOXYETHOXY)ETHYL) ETHER AS SVHC

	CAS 625-45-6 CLP index No 607-312-00-1	C <sub>3</sub> H <sub>6</sub> O <sub>3</sub> MW 90.08	
2	2-methoxyethanol, EGME EC 203-713-7 CAS 109-86-4 CLP index No 603-011-00-4	 C <sub>3</sub> H <sub>8</sub> O <sub>2</sub> MW 76.10	Candidate list
3	1,2-dimethoxyethane, Monoglyme EC 203-794-9 CAS 110-71-4 CLP index No 603-031-00-3	 C <sub>4</sub> H <sub>10</sub> O <sub>2</sub> MW 90.12	Candidate list
4	Bis(2-methoxyethyl) ether Diglyme EC 203-924-4 CAS 111-96-6 CLP index No 603-176-00-2	 C <sub>6</sub> H <sub>14</sub> O <sub>3</sub> MW 134.17	Annex XIV
5	1,2-bis(2-methoxyethoxy)ethane, Triglyme EC 203-977-3 CAS 112-49-2 CLP index No 603-176-00-2	 C <sub>8</sub> H <sub>18</sub> O <sub>4</sub> MW 178.23	Candidate list
6	2-ethoxyethanol ethylene glycol monoethyl ether EGEE EC 203-804-1 CAS 110-80-5 CLP index No 603-012-00-X	 C <sub>4</sub> H <sub>10</sub> O <sub>2</sub> MW 90.1	Candidate list

7	2-ethoxyethyl acetate 2-EEA EC 203-839-2 CAS 111-15-9 CLP index No 607-037-00-7	 C6H12O3 MW 132.1	Candidate list
8	1,2-diethoxyethane EC 211-076-1 CAS 629-14-1 CLP index No 603-208-00-5	 C6H14O2 MW 118.1	Candidate list

## 11.2 Alternatives

Tetraglyme belongs to the group of ethylene glycol ethers (E-series), and among them to the special group of glymes (glycol diethers), which are defined as saturated non-cyclic polyethers containing no other functional groups. Ethylene glycol ethers are used as solvents or functional fluids. Given the structural similarity of these substances as illustrated below, the same technical functions and the overlap between uses within this group, substitution between them seems highly likely.

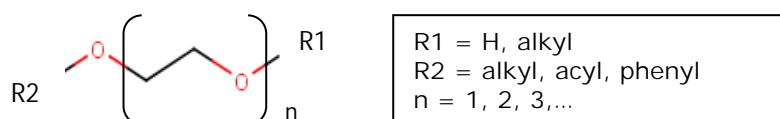


Figure 1: Chemical structure of ethylene glycol ethers.

According to general information from industry glymes offer high solvency, high stability in strong bases and moderate stability in acid solutions. Glymes efficiently solvate cations, increase anion reactivity, and thus can increase both selectivity and reaction rates. Most glymes are water-soluble, but a range of solubility and boiling points is available. The polyether structure produces only weak associations between glyme molecules, and is responsible for the low viscosity and excellent wetting properties of these solvents (information from BASF website<sup>13</sup>). According to BASF, glymes are used as reaction solvents and in closed loop applications such as gas scrubbing and in refrigeration systems. The higher molecular weight glymes are recommended for emissive applications such as coatings, inks, adhesives and in cleaning compounds. The lower molecular weight glymes should not be used in emissive applications due to their reproductive toxicity. The descriptions and possible applications of glymes show that they may be treated as a group with various similar areas of application and hence may in general substitute each other.

<sup>13</sup>[http://www.intermediates.basf.com/chemicals/web/en/function/conversions:/publish/content/news-and-publications/brochures/download/BASF\\_Brochure\\_High-Performance-Solvents.pdf](http://www.intermediates.basf.com/chemicals/web/en/function/conversions:/publish/content/news-and-publications/brochures/download/BASF_Brochure_High-Performance-Solvents.pdf)



However, their difference in physico-chemical parameters like solubility and boiling points has to be considered.

The similar low molecular weight substances mono-, di- und triglyme are already included in the candidate list. Diglyme is also included in Annex XIV. Several applications for authorisations have been made. From the uses applied for diglyme, it is apparent that these are very specific. For this reason, the suitability of alternatives also for tetraglyme needs to be judged case by case depending on the technical functions needed for a certain use.

Possible alternatives may be ethylene glycol ethers with longer initial alkoxy groups as, based on the current knowledge, they are metabolized to alkoxyacetic acids with increasing length (propoxyacetic acid, butoxyacetic acid, hexyloxyacetic acid), which are not linked to reproductive toxicity. As a general rule it seems that with an increase in the length of alkoxy groups the reproductive toxicity effects decrease.

In order to demonstrate this systematically, different longer chain glycol ethers have been compiled and compared to tetraglyme. To get an overview on these possible alternatives their physico-chemical properties, which determine the solvent properties, are compared in Table 8. Especially viscosity, evaporation rate, chemical structure/hydrogen bonding group and solubility parameters might give some hints on possible substitutes. A lubricant should be stable at the conditions of use and crucial properties might be melting/boiling temperature, chemical structure/hydrogen bonding group, surface tension and vapour pressure/evaporation rate. Especially 2-(2-butoxyethoxy)ethyl acetate and 2-(2-butoxyethoxy)ethanol seem to have similar physico-chemical properties as tetraglyme and therefore these substances may be potential substitutes.

Table 9 shows a comparison of their uses registered under REACH giving some first indications on substitution possibilities. Tetraglyme is mainly used as solvent for paints, inks and coatings, as process chemical and as lubricant. Several ethylene glycol ethers show similar use patterns and may therefore be suitable substitutes for one or several uses of tetraglyme.

Also substances of the group of propylene glycol ethers (P-series) may be alternatives for some applications. According to information from industry the E-series glycol ethers are more water soluble and slightly stronger solvents than P-series substances<sup>14</sup>. Propylene glycol ethers are described as more hydrophobic and better solvents for oils and organic chemicals. A trend over the past years has been described by ChemSec in their SIN List showing that E-series glycol ethers have been phased out and progressively been replaced by P-series alternatives whenever possible<sup>15</sup>.

Due to the type of uses of tetraglyme it seems necessary to find process-based and application-based substitutions to meet the desired criteria and properties. Alternatively to chemicals within the group of glycol ethers e.g. phenol ethers like 2-phenoxyethanol and 2-(2-phenoxyethoxy)ethanol or cyclic ethers such as dimethyl isosorbide might be substitutes<sup>16</sup>. The physico-chemical properties of these substances seem to be in a similar margin as those of tetraglyme (see Table 8) and based on the available data on ECHA dissemination site their toxicity seems to be low.

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<sup>14</sup> <https://www.dow.com/content/dam/dcc/documents/en-us/mark-prod-info/324/324-06467-01-glycol-ethersolvents-selection-guide.pdf?iframe=true>

<sup>15</sup> <https://sinlist.chemsec.org/chemical-groups/glycol-ethers/>

<sup>16</sup> <https://www.rivm.nl/en/news/promising-biobased-alternatives-to-substances-of-very-high-concern>

Table 8: Physico-chemical properties of possible alternatives in the E-series and phenol ethers compared to tetraglyme [Source: ECHA Dissemination site (accessed 10.12.2019), Pubchem<sup>17</sup>, Huntsman<sup>18</sup>]

Remark: Depending on the source there may be differences in the values reported.

Identity	Classification		Phys.chem. properties											Solubility parameters # cal/cm <sup>3</sup>			
	Harmonized classification	Self-classification in registration	Molecular Weight g/Mol	Density 25°C g/ml	Water solubility mg/l	Melting point °C	Flash Point °C	Boiling Point 760 mm Hg °C	Evaporation Rate <sup>1</sup> 25°C relative to n-butyl acetate	Viscosity (at 20°C)	Surface Tension dynes/cm	Hydrogen Bonding Group*	Molar Volume cc/gM	SPo	SPd	SPp	SPh
<b>Ethylene Glycol Ethers</b>																	
<a href="#">bis(2-(2-methoxyethoxy) ethyl) ether, tetraglyme</a> EC 205-594-7 CAS 143-24-8	Repr. 1B H360fD	Repr. 1B H360	222.28	1.01	1012000	-30	136 ±2°C at 100.35 kPa	275	-	kinematic viscosity: 3.69 ± 0.01 mm <sup>2</sup> /s dynamic viscosity: 3.73 ± 0.02 mPa.	28.2-34.2	M	221.2	8.7	7.7	1.0	4.0
<a href="#">2-(propyloxy)ethanol</a> EC 220-548-6 CAS 2807-30-9	Acute Tox. 4 * H312 Eye Irrit. 2 H319	Acute Tox. 4 * H312 Eye Irrit. 2 H319 Flam. Liq. 3, H226	104.15	0.911	-	-90	51	150	0.191	2.97 kinematic viscosity (in mm <sup>2</sup> /s)	29.28	M	114.4	12.1	8.5	3.9	7.8

<sup>17</sup><https://pubchem.ncbi.nlm.nih.gov/><sup>18</sup>[https://che.utah.edu/~ring/Design%20I/Articles/Solvents\\_Data%5B1%5D.pdf](https://che.utah.edu/~ring/Design%20I/Articles/Solvents_Data%5B1%5D.pdf)

ANNEX XV – IDENTIFICATION OF BIS(2-(2-METHOXYETHOXY)ETHYL) ETHER AS SVHC

<a href="#">2-butoxyethanol</a> EC 203-905-0 CAS 111-76-2	Acute Tox. 4 * H302 Acute Tox. 4 * H312 Skin Irrit. 2 H315 Eye Irrit. 2 H319 Acute Tox. 4 * H332	Acute Tox. 4 * H302 Acute Tox. 4 * H312 Acute Tox. 4 * H312 Skin Irrit. 2 H315 Skin Irrit. 2 H315 Eye Irrit. 2 H319 Acute Tox. 4 * H332	118.17	0.91	100000	-74.8	67	168	0.072	3.3 mPa · s (dynamic)	26.92	M	131.6	10.2	7.8	2.5	6.0
<a href="#">2-butoxyethyl acetate</a> EC 203-933-3 CAS 112-07-2	Acute Tox. 4 * H312 Acute Tox. 4 * H332	Acute Tox. 4 * H312 Acute Tox. 4 * H332 Acute Tox. 4, H302	160.21	0.94	9000	-63	78	192	0.03	1.81 mPa · s (dynamic)	27.4	M	170.4	10.3	8.6	3.0	4.9
<a href="#">2-(2-(2-butoxyethoxy)ethoxy)ethanol</a> EC 205-592-6 CAS 143-22-6	Eye Dam. 1 H318	Eye Dam. 1 H318	206.28	0.989	-	-30	130	278	0.01	At 25°C: 9.2 mPa · s (dynamic) At 20°C: 61.4mN /m	-	-	-	9.3	7.9	3.4	3.6 §
<a href="#">2-hexyloxyethanol</a> EC 203-951-1 CAS 112-25-4	Acute Tox. 4 * H302 Acute Tox. 4 * H312 Skin Corr. 1B H314	Acute Tox. 4 * H302 Acute Tox. 4 * H312 Skin Corr. 1B H314 Eye Dam. 1, H318 Acute Tox. 3, H311	146.23	0.888	9900	-45.1	91.5	208	0.01	4.4 mPa · s (dynamic)	27.7	M	164.8	11.7	9.0	2.4	7.2
<a href="#">2-(2-butoxyethoxy)ethyl acetate</a> EC 204-685-9 CAS 124-17-4	Not in Annex VI of CLP	Not Classified	204.26	0.977	-	-	102	235-250	0.001	3.5 mPa · s (dynamic)	30.0	M	209.1	11.0	8.1	2.8	6.7
<a href="#">Ethanol, 2-butoxy-, manufacture of, by-products from</a> EC 310-287-7 CAS 161907-77-3		(see 907-996-4)	-	0,992	-	-	-	-	-	-							

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Reaction mass of <a href="#">2-(2-(2-butoxyethoxy)ethoxy)ethan-1-ol</a> ; <a href="#">3,6,9,12-tetraoxahexadecan-1-ol</a> EC - CAS -	Not in Annex VI of CLP	Eye Dam. 1 H318	-	-	-	142	-	-	4 mPa · s (dynamic)	At 20 °C: 61.4							
<a href="#">2-(2-butoxyethoxy)ethanol</a> EC 203-961-6 CAS 112-34-5	Eye Irrit. 2 H319	Eye Irrit. 2 H319	162.23	0.953	100000	-68	114	231	0.003	6 mPa · s (dynamic)	29.37	M	170.6	10.0	7.8	3.4	5.2
<a href="#">2-(2-hexyloxyethoxy)ethanol</a> EC 203-988-3 CAS 112-59-4	Acute Tox. 4 H312 Eye Dam. 1 H318	Acute Tox. 4 H312 Eye Dam. 1 H318	190.28	-	17000	-40	135	260	<0.01	8.26 mPa · s (dynamic)	29.8			9.7	7.8	2.9	4.9 §
<a href="#">3,6,9,12-tetraoxahexadecan-1-ol</a> EC 216-322-1 CAS 1559-34-8	Not in Annex VI of CLP	Eye Irrit. 2 H319	250.33	0.976	-	-33	131	-	-	-	-						
<b>Phenol Ethers</b>																	
<a href="#">2-phenoxyethanol</a> EC 204-589-7 CAS 122-99-6	Acute Tox. 4 H302 Eye Irrit. 2 H319	Acute Tox. 4 H302 Eye Irrit. 2 H319 Skin Irrit. 2 H315 STOT SE 3 H335 Repr. 2 H361	138.17	1.099	25000	9.1	230	237	0.001	20.32	42.30	M	125.7	11.5	6.7	5.1	7.8
<a href="#">2-(2-phenoxyethoxy)ethanol</a> EC 203-227-5 CAS 104-68-7	Not in Annex VI of CLP	Eye Dam. 1 H318 Eye Irrit 2 H319 Acute Tox 4 H302	182.22	1.11	35000	-20	161	296		kinematic viscosity: 40 mm <sup>2</sup> /s	at 20°C: 69.9 Nm/m (1% solution)						

\* M — Moderately hydrogen bonded solvents (ketones, esters, ethers and glycol monoethers); P — Poorly hydrogen bonded solvents (hydrocarbons and halo-, nitro-, and cyano-substituted hydrocarbons), S — Strongly hydrogen bonded solvents (alcohols, amines, acids, amides, and aldehydes).

# Hansen solubility parameters SP<sub>d</sub> (dispersion), SP<sub>p</sub> (polar), and SP<sub>h</sub> (hydrogen bonding) (cal<sup>1/2</sup> cm<sup>-3/2</sup>); SP<sub>o</sub> is calculated by taking the square root of the sum of the squares of the Hansen solubility parameters SP<sub>d</sub>, SP<sub>p</sub>, and SP<sub>h</sub>.

§ Additional sources: technical data sheet CAS 143-22-6: <https://www.dow.com/content/dam/dcc/documents/en-us/productdatasheet/110/110-00972-01-butoxytriglycol-tds.pdf?iframe=true>; technical data sheet CAS 112-59-4: <https://www.dow.com/en-us/document-viewer.html?ramdomVar=9179357895336259513&docPath=/content/dam/dcc/documents/en-us/productdatasheet/110/110-00970-01-hexyl-carbitol-solvent-tds.pdf>

Table 9: Uses of some E-series glycol ethers and phenol ethers according ECHA dissemination site<sup>19</sup> (accessed 06/2020)

EC/List no	Ton. band (reg.) / t	Processing Chemical	Oil & gas field / Mining	Water treatment / applicat. on surface waters	Paints / Coatings / Inks	Adhesives/ Sealants/ Foams/ Polymers	Hydraulic, functional and metal working fluids / lubricants / fuels	de-icing or anti-icing applicat.	Cleaning agents / surface treatment / removers	Construction, building and/or road materials	Articles / Service life
<b>Ethylene Glycol Ethers</b>											
bis(2-(2-methoxyethoxy) ethy) ether, tetraglyme EC 205-594-7, CAS 143-24-8	100-1000	x	x		x		x				x
2-(propyloxy)ethanol EC 220-548-6 CAS 2807-30-9	>1000	x			x				x		
2-butoxyethanol EC 203-905-0 CAS 111-76-2	>1000	x	x	x	x	x	x		x	x	
2-butoxyethyl acetate EC 203-933-3 CAS 112-07-2	>1000				x	x			x		x
2-(2-(2-butoxyethoxy) ethoxy)ethanol EC 205-592-6 CAS 143-22-6	>1000	x	x		x	x	x		x		x
2-hexyloxyethanol EC 203-951-1 CAS 112-25-4	>1000				x	x			x		
2-(2-butoxyethoxy)ethyl acetate EC 204-685-9 CAS 124-17-4	>1000				x						
Ethanol, 2-butoxy-, manufacture of, by-products from EC 310-287-7 CAS 161907-77-3	>1000		x		x		x				
Reaction mass of 2-[2-(2-butoxyethoxy)ethoxy]ethan-1-ol; 3,6,9,12-tetraoxahexadecan-1-ol EC - CAS -	>1000	x	x	x	x		x		x		
2-(2-butoxyethoxy)ethanol EC 203-961-6 CAS 112-34-5	>1000	x	x	x	x	x	x		x	x	x

<sup>19</sup> <https://echa.europa.eu/de/home>

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2-(2-hexyloxyethoxy)ethanol EC 203-988-3 CAS 112-59-4	100-1000	x			x	x	x		x	x	x
3,6,9,12-tetraoxahexadecan-1-ol EC 216-322-1 CAS 1559-34-8	0-10				x		x				
<b>Phenol Ethers</b>											
2-Phenoxyethanol EC 204-589-7 CAS 122-99-6	>1000		x		x		x		x		x
2-(2-Phenoxyethoxy)ethanol EC 203-227-5 CAS 104-68-7	100-1000				x		x		x		

### 11.3 Existing EU legislation

The substance is included in the 15<sup>th</sup> ATP<sup>20</sup> of regulation (EC) No 1272/2008. The substance tetraglyme is harmonized classified in the hazard class toxic for reproduction category 1B (H360FD: May damage fertility. May damage the unborn child) in accordance with the CLP Regulation<sup>21</sup>.

No occupational exposure limits for tetraglyme are available in the EU.

### 11.4 Previous assessments by other authorities

No assessments performed by any other authority are known.

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<sup>20</sup> COMMISSION DELEGATED REGULATION (EU) 2020/1182

<sup>21</sup> Classification in accordance with section 3.7 of Annex I to Regulation (EC) No 1272/2008.

## REFERENCES

### References for Part I

- ECHA (2018). RAC Opinion proposing harmonised classification and labelling at EU level of bis(2-(2-methoxyethoxy)ethyl) ether; tetraglyme, available at <https://echa.europa.eu/documents/10162/8a9a02a0-498f-17e5-683a-f9f303a20c0e>
- EU (2006). Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC. Official Journal of the European Union, L396: 1-849.
- EU (2008). Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packing of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. Official Journal of the European Union, L353: 1-1355.

### References for Part II

- ECHA (2020). ECHA Dissemination site <https://echa.europa.eu/de/information-on-chemicals> (accessed June, 2020).
- EU (2008). Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packing of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. Official Journal of the European Union, L353: 1-1355.
- EU (2020). COMMISSION DELEGATED REGULATION (EU) 2020/1182 of 19 May 2020 amending, for the purposes of its adaptation to technical and scientific progress, Part 3 of Annex VI to Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures.
- Tang S. and Zhao H. (2014). Glymes as versatile solvents for chemical reactions and processes: from laboratory to industry. RSC Adv, 4 (22), 11251-11287. Available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3981120/pdf/nihms568452.pdf>