29 November 2012

Background document for bis(2-methoxyethyl)ether (Diglyme, DEGDME)

Document developed in the context of ECHA's fourth Recommendation for the inclusion of substances in Annex XIV

Information comprising confidential comments submitted during public consultation, or relating to content of Registration dossiers which is of such nature that it may potentially harm the commercial interest of companies if it was disclosed, is provided in a confidential annex to this document.

1. Identity of the substance

Chemical name:	bis(2-methoxyethyl)ether (Diglyme, DEGDME)
EC Number:	203-924-4
CAS Number:	111-96-6
IUPAC Name:	1-methoxy-2-(2-methoxyethoxy)ethane

2. Background information

2.1. Intrinsic properties

Bis(2-methoxyethyl)ether (Diglyme, DEGDME) was identified as a Substance of Very High Concern (SVHC) according to Article 57 (c) as it is classified in Annex VI, part 3, Table 3.1 (the list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008 as toxic for reproduction 1B , H360FD ("May damage fertility. May damage the unborn child.")[1], and was therefore included in the Candidate List for authorisation on 19 December 2011 following ECHA's decision ED/77/2011.

[1] This corresponds to a classification as toxic for reproduction category 2 (R60-61: "May impair fertility; May cause harm to the unborn child") in Annex VI, part 3, Table 3.2 (the list of harmonised classification and labelling of hazardous substances from Annex I to Directive 67/548/EEC) of Regulation (EC) N° 1272/2008

2.2. Imports, exports, manufacture and uses

2.2.1. Volume(s), imports/exports

According to data provided in the registration(s), the amount of the substance manufactured and/or imported into the EU in 2009 was in the range of 100 – 1000 t/y. No information on exports is available.

2.2.2. Manufacture and uses

2.2.2.1. Manufacture and releases from manufacture

On the basis of measured data reported by ECETOC (1995) for other ethylene glycol ethers which are produced in the same way and have similar volatilisation behaviour with diglyme, WHO (2002) estimated time-weighted average (TWA) exposures during the manufacture of diglyme to be in the range of 0.01 and 6.5 ppm[2]. In the WHO report, also a maximum dermal body dose of 0.6 mg/kg bw/day was estimated on the basis of an EASE estimation, assuming that trained workers incidentally have direct skin contact with diglyme during cleaning and maintenance operations (Austria, 2011). Estimated exposures according to the registration dossiers are provided in the confidential annex to this document.

For workers, inhalation DNELs for developmental toxicity as calculated by the registrants and Austria (2011) are 4.8ppm and 2.1 ppm (0.5 ppm for general population) respectively[3]. The difference is especially due to different application of assessment factors. Dermal DNELs have been calculated as 2.08 and 0.8 mg/kg bw/day (0.4 mg/kg bw/day for general population) by registrants and Austria (2011) accordingly. Exposure limits for diglyme are established in some European countries, but no EU-wide indicative occupational exposure limit (IOEL) has been established (Austria, 2011).

2.2.2.2. Uses and releases from uses

Uses

According to information provided in the registration(s) the substance is used at industrial sites as a "**solvent** or **process chemical** and **distribution of substance**". The substance is used in a variety of applications (information from Registration complemented by information in the Annex XV dossier – Austria, 2011 – and from the public consultation on the draft recommendation – RCOM, 2012):

- as solvent for many **syntheses of chemicals and pharmaceuticals**

  For instance, it is used as reaction solvent for Grignard-, reduction-, alkylation-, and organo-metallic reactions, and in general in reactions involving alkali metals such as lithium, sodium and potassium, because of its

[2] Conversion factor for Diglyme (20°C, 1014hPa) (Ecetoc, 2005 in Austria, 2011): 1ppm = 5.579mg/m³

[3] **Note**: Available exposure estimates and DNEL values reported in the current background document intend to give an indication of the magnitude of exposure associated with manufacture and the different uses and do not comprise any assessment of the risk related to the toxicity for reproduction of Diglyme.

dipolar aprotic properties and its chemical stability (Clariant website in Austria, 2011).

- in **extraction**, **distillation**, and **purification** processes

  Diglyme is applied as entrainer for aceotropic distillations, whereby chemical products are purified by distillation or extracted from an azeotropic mixture by distillation (at elevated temperature) (comment #11 in RCOM, 2012). For example it is used for separation of water / acetone mixtures for obtaining purified acetone (Clariant website), or for purification of active pharmaceutical ingredients (RCOM, 2011). According to industry, diglyme is not known to be used in other extraction processes (comment #11 in RCOM, 2012).

- in the production of **plastic and rubber** products

  This includes also the use in the production of magnetic polystyrene beads (Austria, 2011).

- in the production of **binding agents** (according to a 2010 survey of the Austrian Central Labour Inspectorate; Austria, 2011)

- in sealed **batteries** as solvent of electrolytes

- in **PTFE[4] etchant solutions** (comment #8 in RCOM, 2012; Aerospace Industries Association of America in RCOM, 2011; also mentioned at Clariant's website), e.g. for activation of PTFE sealant rings

- **filling and packaging for Scientific Research & Development** (comment #9 in RCOM, 2012)

- potentially **other** applications (see paragraphs below)

During the public consultation, further uses of diglyme were mentioned (Aerospace Industries Association of America in RCOM, 2011), such as in ***rain erosion coatings*** (i.e. coatings used to protect e.g. aircrafts from raindrops hitting the surface at high speeds), in ***electronic coatings*** as specialty thinner, in ***adhesives,*** and in ***syntactic foam*** for filling composite materials. It is so far not clear whether those uses take place also in the EU or only outside the EU, potentially resulting in the incorporation of diglyme in imported articles, such as aerospace and defence products.

Further information on potential applications is available from reports in the literature, including the use in mixtures such as ***paints*** (INERIS, 2007 in Austria, 2011), as well as in the ***production of semiconductor chips***, and in ***automotive care products***, ***lacquers***, ***diesel fuels,*** for ***photolithography***, as ***active pharmaceutical ingredient***, etc. (U.S. EPA, 2003 and WHO, 2002 in Austria, 2011). It is however noted that the substance has been registered only for industrial uses, with uses in any consumer product (apart from sealed batteries) advised against. During the public consultations, industry stated that uses of mixtures intended for consumers are rather historic, due to the current REACH restriction (REACH Annex XVII, entry 30); according to industry, in the context of OSPA (Association of Oxygenated Solvent Producers) Charter on Glycolethers, OSPA member companies request annual declarations from all customers that diglyme will not be used for products placed on the market for

[4] poly tetrafluoro ethylene

sale to the general public, which is a prerequisite for the future supply of the substance (comment #6 in RCOM, 2012).

Volumes per sector of use

According to industry the majority of diglyme (>90%) is used in the chemical and pharmaceutical sectors for large scale industrial processes (synthesis, extraction/distillation) in closed systems (comments #6, 11 in RCOM, 2012).

Releases from uses

No measured data are available on diglyme exposure concentrations at the workplace, apart from a report on six measurements in France between 2000 and 2006 (inhalation exposure by professionals) which were probably[5] non-conclusive of an inhalation exposure (AFSSET in Austria, 2011). On the basis of measured data reported by ECETOC (1995) for other ethylene glycol ethers with similar uses and similar volatilisation behaviour as diglyme, WHO (2002) estimated time-weighted average (TWA) air concentrations up to 0.5ppm[6] in the semiconductor industry, and up to 5.6ppm during painting operations (Austria, 2011)[7]. It has though not been confirmed that those specific uses take currently place in the EU.

For most of its uses the substance is expected to be used in closed systems. The PROC categories in registration dossiers indicate closed processes, but also include processes where opportunity for exposure arises (PROC 4), as well as transfer processes (PROCs 8,9) and to some extent production of articles (PROC 14). Apart from the main use (synthesis and extraction/distillation), further uses of diglyme include uses reported to be performed in closed-loop applications, such as in the production of batteries (as solvent of electrolytes; no process description available) and in PTFE etchant solutions (comment # 8 in RCOM, 2012); as well as further uses for which no details are available, such as production of binding agents and production of plastic and rubber products.

No distinction is made between the various applications as solvent / process chemical, but rather a generic exposure scenario has been developed for registration. Estimated exposures according to the registration dossiers are provided in the confidential annex to this document.

The most significant potential for occupational exposure is probably associated with cleaning, maintenance, sampling, and transfer operations (mainly dermal – it is noted that diglyme penetrates many glove materials; gloves made of nitrile and butyl rubber or neoprene are reported to provide the best protection; Austria, 2011). Exposure via inhalation can also not be excluded, although the substance seems to have relatively low volatility, at least at ambient temperature (Diglyme's boiling point and stability make it an ideal solvent for reactions e.g. above 100°C; high temperature is also required for recycling diglyme by distillation). Industry highlighted that especially in high-temperature applications closed systems are essential, for avoiding losses of diglyme and manufactured substances (RCOM, 2012). Here it should though be noted that systems/processes (mainly in smaller

[5] in total 5,558 measurements were performed of professional exposure to glycol ethers, 6 of which for Diglyme; no figures for professional exposure to Diglyme are reported in the AFSSET report, therefore it is assumed that the specific six measurements were non-conclusive of inhalation exposure

[6] Conversion factor for Diglyme (20°C, 1014hPa) (Ecetoc, 2005 in Austria, 2011): 1ppm = 5.579mg/m³

[7] Some information on calculated DNELs is provided in section 2.2.2.1 (Manufacture and releases from manufacture)

scale applications) not designed to recycle diglyme effectively may be subject to potential dermal or inhalation occupational exposure, e.g. due to handling of unrecovered solvent or due to vapour emissions from not effectively enclosed systems.

Exposure during activities such as cleaning, maintenance, sampling, and transfer seems to be difficult to control as even with the suggested operational conditions the Risk Characterization Ratios in the Registration's CSR are close to indicate risk, especially taking into account the uncertainties expressed in the Annex XV Dossier on the values of the derived DNELs (see also RCOM, 2011; response to comment # 2 therein: http://echa.europa.eu/documents/10162/8432b580-d238-4001-ad21-c561fbf73e10).

Furthermore, as there is some uncertainty on the exact sectors and applications in which the substance is used as a solvent / process chemical, as well as on the actual process involved in some of the confirmed applications, there may be other processes in non closed-loop applications with potential for exposure.

Finally, to the extent uses of mixtures such as paints/coatings (professional or industrial) containing diglyme take place in the EU, workers could be exposed, for example during painting/coating operations. However, such uses appear not to be covered by the registrations, based on the PROCs in registrations and the absence of identified professional uses.

Industry has referred to implementation of Risk Management Measures such as use of suitable gloves, special couplings of transfer pipes, and LEV, along with good working procedures and training; highlighting that the great majority of diglyme is used in industries where control of exposure and contamination is well-understood and practiced (RCOM, 2012). Here it is noted that, although such measures play indeed an important role in preventing workers' exposure, they comprise measures which are low in the hierarchy of controls. The effectiveness of such measures in preventing exposure to workers is strongly dependent upon correct application of measures (such as PPE and work practices) by workers, adequate training and continuous supervision. Because proper implementation of these measures throughout the supply chain is therefore not guaranteed, the verification of the effectiveness is questionable.

Monitoring data indicate that the general population may be exposed to diglyme via inhalation of emissions from vehicles and ingestion of contaminated drinking water (HSDB and IKSR in Austria, 2011). On the other hand, the substance is moderately persistent in the environment, while it significantly adsorbs to activated sludge. Monitoring data in river water, ground water, and outflow of STP (Austria, 2011) actually indicate that the risk for man via the aquatic environment is probably low.

2.2.2.3. Geographical distribution and conclusions in terms of (organisation and communication in) supply chain

No concrete information on use sites in the EU is available. Based on the available information, it appears that, in particular for uses in the scope of authorisation, the supply chains contain a small number of EU manufacturers and importers, and an unknown, but presumably at least medium number of downstream users.

2.3. Availability of information on alternatives[8]

According to Ketttenis, 2005 (in Austria, 2011), in general toxic ethylene glycol ethers can only be replaced (in their solvent applications) easily with less toxic propylene glycol ethers which have similar physicochemical properties (in Austria, 2011). No substitutes for present industrial uses of diglyme are reported to be available (communication with OSPA, May 2010, in Austria, 2011). OSPA further states that in general their members pay particular attention to promoting alternatives to glycol ethers classified as "toxic for reproduction". OSPA has therefore been recommending a policy to limit the market of these glycol ethers to industrial applications for which a substitute solution does not yet exist (Austria, 2011).

According to one company butyl diglyme (EC No 204-001-9) can substitute diglyme in Grignard reactions (website of Clariant in the Annex XV dossier, Austria, 2011). Butyl diglyme is not listed in part 3 of Annex VI of the CLP Regulation. The substance may generate explosive peroxides and it may cause skin and eye irritation and irritation of the respiratory tract. No data on the reproductive toxicity of dibutyl glyme are available. According to Directive 2004/42/EC butyl diglyme (boiling point 256°C) is no VOC (Austria, 2011).

An Austrian insurance organisation stated, during the public consultation on identification of Diglyme as SVHC, that similar solvents with less concerning properties are at the market, which though were not specified (RCOM, 2011).

2.4. Existing specific Community legislation relevant for possible exemption

There seems to be no specific Community legislation in force that would allow consideration of an exemption(s) of (categories of) uses from the authorisation requirement on the basis of Article 58(2) of the REACH Regulation.

2.5. Any other relevant information (e.g. for priority setting)

No information available.

[8] Please note that this information was not used for prioritisation.

3. Conclusions and justification

3.1. Prioritisation

Verbal-argumentative approach

Practically the complete amount in the EU is used as solvent in applications in the scope of authorisation, apart from minor uses such as laboratory uses for SRD, or in medicinal products exempted according to Art. 2(5a) of REACH. Therefore Diglyme is used in relatively high volume in the scope of authorisation.

The number of use sites is unknown, but based on available information on the use pattern it appears that the substance is used at least at a medium number of sites. The potential for uncontrolled occupational exposure may in many cases be relatively limited. At the same time there are also aspects which indicate that control of risks may not be obvious in all cases, and that the proper implementation of RMM such as suitable gloves and LEV is very often essential. Significant dermal or even inhalation exposure may for instance occur in occupational activities during maintenance/cleaning/sampling/transfer operations, in particular in less modern facilities. Exposure during such activities seems to be difficult to control as even with the suggested operational conditions the RCRs are close to indicate risk. There is also uncertainty regarding potential exposure during some of the applications as solvent / process chemical, as the overall information on actual applications in the EU (or the processes involved in confirmed applications) is somewhat vague.

Scoring approach

Score			Total Score
Inherent properties (IP)	Volume (V)	Uses - wide dispersiveness (WDU)	(= IP + V + WDU)
Score: 0 (Toxic for reproduction 1B)	Score: 5 (Relatively high volume within the scope of authorisation)	Overall score: 6-9 Site-#: 2-3 (Use at an unknown, but presumably at least medium number of sites) Release: 3 (Exposure to workers may be controlled in many instances, but may be significant for example during maintenance, cleaning, sampling, and transfer operations)	11-14

Conclusion, taking regulatory effectiveness considerations into account

On the basis of the prioritisation criteria bis(2-methoxyethyl) ether gets moderate to relatively high priority for inclusion in Annex XIV.
The substance is used in a relatively high volume and apparently many applications. It appears that some of the process steps taking place during the uses have a potential for significant occupational exposure and that this exposure

is difficult to control, as risk characterisation ratios close to risk (even for the suggested operational conditions) indicate.

Therefore, it is proposed to recommend bis(2-methoxyethyl) ether (Diglyme) for inclusion in Annex XIV.

4. References

Austria (2011): Annex XV dossier for the proposal for identification of bis(2-methoxyethyl)ether as a category 1A or 1B CMR, PBT, vPvB or a substance of an equivalent level of concern. Submitted by Environment Agency Austria on behalf of the Austrian Competent Authority (Austrian Federal Ministry of Agriculture, Forestry, Environment and Water Management) in cooperation with Belgian Competent Authority (Belgian Federal Public Service (FPS) Health, Food Chain Safety and Environment, Risk Management Service) and Polish Competent Authority (Bureau for Chemical Substances).

http://echa.europa.eu/documents/10162/807172a7-fb9b-4fa3-bf41-6d13e99b56d1

RCOM (2011): "Responses to comments" document compiled by the Austrian CA from the commenting period 29/08/2011 – 13/10/2011 on the identification of bis(2-methoxyethyl)ether as SVHC.

http://echa.europa.eu/documents/10162/8432b580-d238-4001-ad21-c561fbf73e10

RCOM (2012): "Responses to comments" document compiled by ECHA from the commenting period 20/06/2012 – 19/09/2012 on the draft 4th recommendation for inclusion of substances in Annex XIV of REACH, for the substance bis(2-methoxyethyl)ether.

http://echa.europa.eu/documents/10162/13640/axiv_4th_recommendation_bis_2_methoxyethyl_ether_diglyme_rcom_en.pdf