Annex XV dossier

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE AS A CMR CAT 1 OR 2, PBT, vPvB OR A SUBSTANCE OF AN EQUIVALENT LEVEL OF CONCERN

Substance Name(s): 2-Ethoxyethanol (ethylene glycol monoethyl ether; EGEE)

EC Number(s): 203-804-1

CAS Number(s): 110-80-5

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 the Belgian Federal Public Service (FPS) Health, Food Chain Safety and Environment, Risk Management Service

and the Polish Bureau for Chemical Substances and Preparations

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TABLES

LIST OF ABBREVIATIONS

AFSSET	**French Agency for Environmental and Occupational Health Safety, now "ANSES", Agence nationale de sécurité sanitaire**
CMR	**Carcinogenic, Mutagenic or toxic to Reproduction**
EASE	**Estimation and Assessment of Substance Exposure**
EEP	**Ethyl-3-ethoxypropion**
EGBE	**2-Butoxyethanol**
EGBEA	**2-Butoxyethyl acetate**
EGEE	**2-Ethoxyethanol**
EGME	**2-Methoxyethanol**
EGPE	**ethylene glycol monopropyl ether**
EGPEA	**ethylene glycol monopropyl ether acetate**
EU RAR	**European Union Risk Assessment Report**
INRS	Institut National de Recherche et de Sécurité
IOELV	Indicative Occupational Exposure Limit Value
IUCLID	**International Uniform Chemical Information Database**
OEL	**Occupational Exposure Limit**
OSPA	**Oxygenated Solvents Producers Association**
MOS	**Margin of Safety**
PGME	**1-Methoxy-2-propanol**
PGMEA	**1-Methoxy-2-propyl acetate**
PBT	**Persistent, Bioaccumulative and Toxic**
SCOEL	**Scientific Committee on Occupational Exposure Limits**
SME	**Small and medium enterprises**
SPIN	**Substances in Preparations in the Nordic countries**
STEL	**Short Term Exposure Level**
TRGS	**Technische Regeln für Gefahrstoffe; Technical rules for Hazardous substances**
TWA	**Time Weighted Average**
vPvB	**Very Persistent and very Bioccumulative**

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE AS A CMR CAT 1 OR 2, PBT, VPVB OR A SUBSTANCE OF AN EQUIVALENT LEVEL OF CONCERN

Substance Name(s): 2-Ethoxyethanol (ethylene glycol monoethyl ether; EGEE)

EC Number(s): 203-804-1

CAS number(s): 110-80-5

- The substance is proposed to be identified as substance meeting the criteria of Article 57 (c) of Regulation (EC) 1907/2006 (REACH) owing to its classification as toxic for reproduction 1B.

Summary of how the substance meets the CMR (Cat 1 or 2), PBT or vPvB criteria, or is considered to be a substance giving rise to an equivalent level of concern

2-Ethoxyethanol (EGEE) is listed as entry 603-012-00-X 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) No 1272/2008 as toxic to reproduction, category 2[1].

Therefore, this classification of the substance(s) in Regulation (EC) No 1272/2008 shows that the substance meets the criteria for classification as toxic for reproduction in accordance with Article 57 (c) of REACH.

Registration number(s) of the substance or of substances containing a given constituent/impurity or leading to the same transformation or degradation products:

Not relevant.

[1] This corresponds to a classification as toxic for reproduction (1B) in Annex VI, part 3, Table 3.1 of Regulation (EC) No. 1272/2008 (list of harmonised classification and labelling of hazardous substances)

PART I

JUSTIFICATION

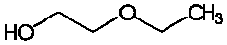
1 IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

1.1 Name and other identifiers of the substance

Table 1: Substance identity

EC number:	203-804-1
EC name:	2-Ethoxyethanol
CAS number (in the EC inventory):	110-80-5
CAS number:	110-80-5
CAS name:	Ethanol, 2-ethoxy-
IUPAC name:	2-Ethoxyethanol
Index number in Annex VI of the CLP Regulation	603-012-00-X
Molecular formula:	C4H10O2
Molecular weight range:	90.1 g/mol
Synonyms:	Ethylene glycol monoethyl ether; EGEE

Structural formula:



1.2 Composition of the substance

Name: 2-Ethoxyethanol

Description:

Degree of purity: > 99 % w/w

Table 2: Constituents

Constituents	Typical concentration	Concentration range	Remarks
2-Ethoxyethanol EC No: 203-804-1	> 99 % w/w		

Table 3: Impurities

Impurities	Typical concentration	Concentration range	Remarks
unknown impurities	< 1 % w/w		
acetic acid; EC No: 200-580-7	< 0.005 % w/w		

1.3 Physico-chemical properties

Table 4: Overview of physicochemical properties

Property	Value	References
Physical state at 20°C and 101.3 kPa	Colourless liquid	
Melting/freezing point	< - 80 °C	Ullmann, 1978
Boiling point	132 - 137 °C at 1013hPa	Ullmann, 1978
Vapour pressure	5.3 hPa at 20 °C	Kirk-Othmer, 1980
Water solubility	miscible in each ratio at 20 °C	Kirk-Othmer, 1980
Partition coefficient n-octanol/water (log value)	log Pow –0.54 to –0.10 [1)]	Dearden & Bresnen, 1988
Dissociation constant		
Relative density	0.930 at 20 °C	Ullmann, 1978
Surface tension	69.5 mN/m at 25 °C [2)]	Union Carbide, 1998
Flash point	40 °C (closed cup)	Chemsafe, 1996
Flammability	flammable [3)]	Chemsafe, 1996
Ignition temperature	235 °C	Chemsafe, 1996
Explosive properties	not explosive [4)]	Chemsafe, 1996
Oxidising properties	no oxidising properties [5)]	Chemsafe, 1996
Henry's law constant	0.003 Pa * m³ * mol-1	Howard, Meylan; SRC 1993

1) a log Pow of – 0.43 was used in the EU RAR draft, 2008
2) Ring method
3) Test A.10 not conducted (substance is a liquid) Test A.12 and A.13 not conducted because of structural reasons
4) No test conducted because of structural reasons
5) No test conducted because of structural reasons

2 HARMONISED CLASSIFICATION AND LABELLING

2-Ethoxyethanol is classified and labelled according to Annex VI of Reg. (EC) No 1272/2008, Annex VI, Table 3.1. as follows:

Index Number: 603-012-00-X

Hazard class and category codes

Flam. Liq. 3

Repr. 1B

Acute Tox. 4 *[2]

Acute Tox. 4 *

Acute Tox. 4 *

Hazard statement codes

H226

H360-FD

H332

H312

H302

Pictogram, signal word codes

GHS02

GHS08

GHS07

Dgr

[2] Minimum classification for a category is indicated by the reference * in the column 'Classification' in Table 3.1.

For certain hazard classes, including acute toxicity and STOT repeated exposure; the classification according to the criteria in Directive 67/548/EEC does not correspond directly to the classification in a hazard class and category under this Regulation. In these cases the classification in this Annex shall be considered as a minimum classification. This classification shall be applied if none of the following conditions are fulfilled:

— the manufacturer or importer has access to data or other information as specified in Part 1 of Annex I that lead to classification in a more severe category compared to the minimum classification. Classification in the more severe category must then be applied;

— the minimum classification can be further refined based on the translation table in Annex VII when the physical state of the substance used in the acute inhalation toxicity test is known to the manufacturer or importer. The classification as obtained from Annex VII shall then substitute the minimum classification indicated in this Annex if it differs from it.

Hazard statement codes

H226

H360FD

H332

H312

H302

Specific Conc. Limits; M-factors; Notes: none

Classification and Labelling of EGEE according to Reg. (EC) No 1272/2008, Annex VI, Table 3.2:

Index Number: 603-012-00-X

Classification

R10

Repr. Cat. 2; R60-61

Xn; R20/21/22

Labelling

T

R: 60-61-10-20/21/22

S: 53-45

EGEE is included in a list of substances with harmonised classifications already agreed by the Technical Committee for Classification and Labelling but not included in Annex VI of Regulation (EC) No 1272/2008[3]:

R10

Repr. Cat. 2; R60-61

Xn; R20/22

(deletion of R21)

[3] RAC/07/2009/40: Seventh Meeting of the Risk Assessment Committee, 30 June - 3 July 2009, Helsinki, Finland

3 ENVIRONMENTAL FATE PROPERTIES

Not relevant for this type of dossier.

4 HUMAN HEALTH HAZARD ASSESSMENT

4.1 Toxicity for reproduction

On the summary and discussion of reproductive toxicity according to the EU RAR draft, 2008 see Annex.

5 ENVIRONMENTAL HAZARD ASSESSMENT

Not relevant for this type of dossier.

6 CONCLUSIONS ON THE SVHC PROPERTIES

6.1 CMR assessment

2-Ethoxyethanol (EGEE) is listed as entry 603-012-00-X 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) No 1272/2008 as toxic to reproduction, category 2. This corresponds to a classification as toxic for reproduction (1B) in Annex VI, part 3, Table 3.1 of Regulation (EC) No. 1272/2008 (list of harmonised classification and labelling of hazardous substances).

Therefore, this classification of the substance(s) in Regulation (EC) No 1272/2008 shows that the substance meets the criteria for classification as toxic for reproduction in accordance with Article 57 (c) of REACH.

PART II

INFORMATION ON USE, EXPOSURE, ALTERNATIVES AND RISKS

INFORMATION ON MANUFACTURE, IMPORT/EXPORT AND USES – CONCLUSIONS ON EXPOSURE

1 INFORMATION ON EXPOSURE

1.1 Information on volumes

The EU RAR draft, 2008 indicated that there is one production site of EGEE remaining in the EU. According to recent information from OSPA (Oxygenatd Solvents Producers Association, 2010) the only former producer of EGEE in the EU inside OSPA has ceased production in 2007 and does not intend to register it under REACH. There is no explicit data available on import from outside of the EU (for information on preregistration see chapter 1.1.2). No information is available on possible exports of EGEE. In the EU, the production quantity has declined during the years 2002 – 2006 from 1360 t to 100 t (520 t in 2005 to 100 t in 2006). (EU RAR draft, 2008).

1.1.1 Information from Product Register Data (SPIN database)

The SPIN database[4] (Substances in Preparations in the Nordic countries) was searched for information on EGEE in products on the national markets of Norway, Sweden, Finland and Denmark (see Tables 5 and 6). A general decreasing trend can be observed from 244.8 t in 2005 to 42.8 t in 2008. However, the single figures show that volumes are quite constant in Denmark (with the number of preparations decreasing) and Norway. No clear trend is observed in Finland. Further there is a decreasing number of preparations in Sweden, with quite constant volumes.

[4] http://195.215.251.229/Dotnetnuke/ Please note: The total amount of a substance included in the SPIN database is the added quantity of the substance in all products without the amount of substances exported. Therefore, if a substance is registered first as the imported raw material and then again as part of the final preparation the quantity will be counted twice. Substances which are imported and then used for the formulation of chemical products, which is very often the case in the Nordic countries, will thus be accounted for with up to double the actual amount. Therefore, the tonnages in Table 1 might be considered as overestimations. “0.0 tons” means that the notified volumes were smaller than 0.1 ton.

Table 5: 2-Ethoxyethanol in products according to SPIN for 2005 – 2006

Country	**2005**		**2006**	
	Number of preparations	**Tonnage**	**Number of preparations**	**Tonnage**
Denmark	47	43.5	41	41.9
Finland	6	200.1	6	0.1
Norway	6	0.2	-	-
Sweden	18	1.0	13	1.0

Total: 244.8 tons 43 tons

Table 6: 2-Ethoxyethanol in products according to SPIN for 2007 – 2008

Country	**2007**		**2008**	
	Number of preparations	**Tonnage**	**Number of preparations**	**Tonnage**
Denmark	38	41.8	37	42.5
Finland	5	100.1	4	0.1
Norway	6	0.7	6	0.2
Sweden	12	2.0	10	0.0

Total: 144.6 tons 42.8 tons

1.1.2 Information on 2-ethoxyethanol quantities from pre-registration data

An excerpt from pre-registration shows that 170 companies pre-registered 2-ethoxyethanol 261 times. In order to obtain an estimation of 2-ethoxyethanol quantities in the next years, pre-registration data were analyzed. The results of the pre-registered tonnages and companies are summarized in Table 7.

Table 7: Information on 2-ethoxyethanol tonnages according to pre-registration data

No. of companies	170
No. of companies pre-registrations	261
min t/a acc. no. of pre-registrations	7543 t/a
max t/a acc. no. of pre-registrations	39430 t/a

For pre-registration each company had to indicate the tonnage band (1-10 t/a, 10-100 t/a, 100-1.000 t/a, and 1.000+ t/a) of the actual amount of produced and / or imported 2-ethoxyethanol.

For the estimation of annual tonnages each tonnage band (minimum and maximum amount) is multiplied with the number of pre-registrations and then summed up to give the total amount of imported and / or produced tonnage of 2-ethoxyethanol per year.

This estimate results in a minimum of **7543 t/a** and a maximum of **39430 t/a** of 2-ethoxyethanol imported and/ or produced in Europe. **It is noted that these estimates based on pre-registration data are not entirely reliable and represent only very rough estimates.**

1.1.3 Information from other Member States

Poland

According to data collected by the Polish Bureau for Chemical Substances and Preparations three companies place on the Polish market 39 mixtures containing 2-ethoxyethanol. The total tonnage of mixtures, starting from 2005 to 2010, is around 2360 kg. One company informed on the intention to import 4920 kg of 2-ethoxyethanol itself in 2010.

France

In a report by AFSSET (2008) it is described that the use of EGEE in France has considerably decreased during the last decades (period '2000-2006' compared with period '1987-1998'), but some uses are still remaining (24 preparations declared in SEPIA[5] between 2000 and 2006). According to the report the European production of glycol ethers in general had slightly increased between 2000 and 2006, whereas the partition between E- (based on ethylene oxide) series and P-series (based on propylene oxide) glycols had changed. In 2006, SICOS (French Association of the Organic Chemistry and Biochemistry Industries) posted an annual European production of about 650 000 tons (40% E-series, 60% P-series). In 2000, the annual European production was stated with about 500 000 tons (60% E-series, 40% P-series) (Ministère de la santé, internet consultation, 2007). The glycol ethers EGME and EGEE were produced only in smaller amounts (2005: 3000 tons EGME, 500 tons EGEE).

Conclusion

In the EU, the production quantity has declined during the years 2002 – 2006 from 1360 t to 100 t (520 t in 2005 to 100 t in 2006). A decreasing trend of EGEE use in products can be observed too from 244.8 t in 2005 to 42.8 t in 2008 from the SPIN data. According to recent information from OSPA (Oxygenatd Solvents Producers Association, 2010) the only former producer of EGEE in the EU inside OSPA has ceased production in 2007 and does not intend to register it under REACH. However, an excerpt from pre-registration shows that 170 companies pre-registered 2-ethoxyethanol 261 times. An estimate of volumes results in a minimum of **7543 t/a** and a maximum of **39430 t/a** of 2-ethoxyethanol imported and/or produced in Europe. More reliable data on production/import are expected to become available after the first registration deadline (December 1st, 2010). Such information may be taken into account during the consultation phase.

[5] The SEPIA database of the INRS relates to the chemical preparations placed on the French market. The Registration in this confidential database is mandatory for very toxic, toxic, and corrosive chemical mixtures and for biocides.

1.2 Information on uses

According to the EU RAR draft, 2008 the main proportion (80 %) of EGEE is processed to intermediates such as the 2-ethoxyethanol tert-butyl ether (1-Ethoxy-2-tert-butoxyethane) in chemical industry. The smaller part (20 %) is used as industrial solvent. There is no information on remaining wide dispersive use of 2-ethoxyethanol outside the chemical industry. The current use pattern is as follows (Table 8):

Table 8: Uses and Mass balance of EGEE

	Industrial category (IC)	**Use category (UC)**	**Mass balance [in % of use]**
Non-dispersive use (1)	Chemical industry (3)	Intermediate (33)	80
Non-dispersive use (1)	Chemical industry (3)	Solvent (48)	20

Previously the substance was widely used in open systems, such as paints for private use, in surface treatment of metals and in repair industry. Besides the industrial use as intermediate and solvent, EGEE was used for the formulation of paints, lacquers, varnishes and printing inks. An additional use for 2-ethoxyethanol as anti-freeze additive for aviation fuels and for clearing runways is obsolete now (EU RAR draft, 2008).

Germany

According to the German exposure database MEGA[6] following substance relevant exposure scenarios have been identified for the period from 2000 to 2009: wood processing, electro-techniques, metal processing, production and processing of plastics, offices, painting, coating, printing applications.

According to the German Washing and Cleansing Agents Act information on ingredients and expected production quantities is supplied to the German Federal Environmental Agency. A use of 75 t/a of 2-ethoxyethanol for the application as industrial solvent is registered there (UBA 2006 in EU RAR draft, 2008).

France

In a report by AFSSET (2008) the worker exposures are described as less frequent, but still high and exceed the OEL of 19 mg/m^3 in 5% of cases. It is mainly in the sector of metal working and to a lesser extent in the rubber and plastic industry, in cleaning and printing operations (flexography, serigraphy) (monitoring data collected between 2000 and 2006). The report further refers to following investigations carried out on glycol ethers: An investigation on use in garages, cleaning, hairdressing and general mechanics, carried out in 123 SMEs, has

6 Exposure database MEGA "Measurement data relating to workplace exposure to hazardous substances" - MEGA is a compilation of data gathered through atmospheric measurements and material analyses. Institute for Occupational Safety and Health of the German Social Accident Insurance, Sankt Augustin/Germany (http://www.dguv.de/ifa/en/gestis/mega/index.jsp)

not shown any use of 2-ethoxyethanol (Beaujean et al., 2005). A study on solvents carried out in 2004 by the INRS has not identified 2-ethoxyethanol either (Triolet, 2005). The last investigations carried out by DGCCRF (Direction Générale de la Concurrence, de la Consommation, et de la Répression des Fraudes) in 2006 on paints, varnishes and wide-spread drugstore-products, have not shown any glycol ethers classified as toxic to reproduction, including 2-ethoxyethanol (Communication DGCCRF 2007 from AFSSET). Concerning mixtures, glycol ethers classified as toxic to reproduction are practically not found in marketed mixtures (see Table 9). In total, out of the 13 000 formulations notified in the SEPIA database between 2000 and 2006, only 142 formulations (1% of all) contain glycol ethers considered as toxic to reproduction (cat 2). Amongst those 142 formulations, 82 contain impurities of PGME or PGMEA of which 78 have a concentration lower than 0,5% and 2 a concentration between 0,5 and 3%. **Thus, there are around 60 formulations with considerable content of glycol ethers toxic to reproduction listed in the SEPIA database of the INRS and amongst them, 24 formulations which contain 2-ethoxyethanol.**

Table 9: Number of occurrence of glycol ether mixtures registered in SEPIA between 2000 and 2006

Product category	Totally registered mixtures	Total number of mixtures containing glycol ethers	Total number of mixtures containing glycol ethers classified as "Repr. Cat 2"
paints, varnishes, inks for printing and associated products	1790	809	76
Diverse	1709	159	25
Biocides	4220	363	23
construction material	212	13	3
products for caoutchouc (rubber) and plastics	237	14	2
products for household and industrial cleaning	2129	360	2
products for metallurgic and mechanic use	1121	234	2
prod. for industrial textiles and dyeing	86	31	1
glues and associated products	325	21	1
not specified	-	-	7

Number of occurrence of glycol ethers classified as toxic for reproduction (Cat 2) in mixtures registered in SEPIA between 2000 and 2006. A mixture can be counted several times if several uses are reported or if it contains several glycol ethers classified as Reprotox Cat.2.

Poland

According to data from an industry survey, collected by the Bureau for Chemical Substances and Preparations in Poland for the observation period 2005 – 2010, EGEE is used in the following chemical product categories: coatings and paints, thinners, paint removers, metal surface treatment products, including galvanic and electroplating products. The process categories mentioned by industry are: use in batch and other process (synthesis) where opportunity for exposure arises, mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact) and use as laboratory reagent.

Austria

In 2010 an inquiry was carried out by the Austrian Central Labour Inspectorate among 102 Austrian companies from the industrial sector chemistry/paint and varnish production on the use of seven glycol ethers (reprotoxic cat.2), EGEE being one of them. In total 15 % of all answers were positive, indicating that one or more of the glycol ethers were still in use. EGEE was used by one manufacturer as building block for the production of binding agents. In the finished binding agents the content of the substance was reported to be less than 0.1 %. The results of the inquiry show that the use of the seven glycol ethers at Austrian workplaces in the examined branch is significantly declining.

Uses according to the SPIN database

The SPIN database was searched for industrial uses of 2-ethoxyethanol. Data could be obtained from Denmark, Finland and Norway. The industrial uses are presented in Table 10.

Table 10: Industrial Uses according to the SPIN database

Country	Year	Code	Industrial Use	#Prep**	Tons*
DK	2008	C25	Manufacture of fabricated metal products, except machinery and equipment	14	40.0
DK	2008	C30	Manufacture of other transport equipment	8	0.5
DK	2008	F43	Specialised construction activities	7	0.0
DK	2008	F41	Construction of buildings	6	0.0
DK	2008	F42	Civil engineering	6	0.0
FIN	2008	C21	Manufacture of basic pharmaceutical products and pharmaceutical preparations		
FIN	2008	C25	Manufacture of fabricated metal products, except machinery and equipment		
FIN	2008	H52	Warehousing and support activities for transportation		
DK	2007	28	Manufacture of fabricated metal products, except machinery and equipment	14	40.0
N	2007	35	Manufacture of other transport equipment n.e.c.	4	0.7
DK	2007	36	Manufacture of furniture; manufacturing n.e.c.	4	0.2
DK	2007	35	Manufacture of other transport equipment n.e.c.	8	0.1
DK	2007	45	Construction	9	0.0
FIN	2007	24	Manufacture of chemicals and chemical products		

FIN	2007	28	Manufacture of fabricated metal products, except machinery and equipment		
FIN	2007	63	Supporting and auxiliary transport activities; activities of travel agencies		
DK	2006	28	Manufacture of fabricated metal products, except machinery and equipment	13	40.0
DK	2006	36	Manufacture of furniture; manufacturing n.e.c.	4	0.2
DK	2006	35	Manufacture of other transport equipment n.e.c.	6	0.2
DK	2006	45	Construction	9	0.0
FIN	2006	24	Manufacture of chemicals and chemical products		
FIN	2006	28	Manufacture of fabricated metal products, except machinery and equipment		
FIN	2006	63	Supporting and auxiliary transport activities; activities of travel agencies		
DK	2005	28	Manufacture of fabricated metal products, except machinery and equipment	12	40.1
DK	2005	35	Manufacture of other transport equipment n.e.c.	8	0.7
DK	2005	36	Manufacture of furniture; manufacturing n.e.c.	5	0.3
DK	2005	45	Construction	7	0.0
FIN	2005	24	Manufacture of chemicals and chemical products		
FIN	2005	28	Manufacture of fabricated metal products, except machinery and equipment		
FIN	2005	63	Supporting and auxiliary transport activities; activities of travel agencies		

*The information “0.0 tons” means that the volume is less than 100 kg in Sweden in that particular branch of industry. The tonnage information is always “net” ton = tons imported + tons produced – tons exported.
**The reason for the lack of information on the number of preparations and tons particularly for Finland is that data are kept confidential if the substance is a component in less than 4 preparations.

The industrial use category with the highest volumes (DK, 40 tons/year) is given as “Manufacture of fabricated metal products, except machinery and equipment”.

Additionally, the SPIN database was searched for use categories of 2-ethoxyethanol in Norway, Sweden, Finland and Denmark. The use categories are presented in Table 11.

Table 11: Use categories (UC62) according to the SPIN database

Country	Year	Code	Use category	# Prep**	Tons*
DK	2008	59	Paints, laquers and varnishes	12	0.5
DK	2008	02	Adhesives, binding agents	4	0.1
FIN	2008	34	Laboratory chemicals		
FIN	2008	41	Pharmaceuticals		
FIN	2008	55	Others		
FIN	2008	59	Paints, laquers and varnishes		
S	2007	59	Paints, laquers and varnishes	3	2.0
N	2007	59	Paints, laquers and varnishes	4	0.7
DK	2007	59	Paints, laquers and varnishes	12	0.2
DK	2007	02	Adhesives, binding agents	4	0.0
FIN	2007	09	Cleaning/washing agents		
FIN	2007	34	Laboratory chemicals		
FIN	2007	41	Pharmaceuticals		
FIN	2007	50	Surface-active agents		
FIN	2007	55	Others		
FIN	2007	59	Paints, laquers and varnishes		
DK	2006	43	Process regulators	4	12.0
S	2006	59	Paints, laquers and varnishes	3	1.0
DK	2006	59	Paints, laquers and varnishes	10	0.2
DK	2006	02	Adhesives, binding agents	4	0.0
DK	2006	20	Fillers	4	0.0
FIN	2006	09	Cleaning/washing agents		
FIN	2006	34	Laboratory chemicals		
FIN	2006	41	Pharmaceuticals		
FIN	2006	48	Solvents		
FIN	2006	50	Surface-active agents		
FIN	2006	55	Others		
FIN	2006	59	Paints, laquers and varnishes		

DK	2005	59	Paints, laquers and varnishes	10	0.9
DK	2005	20	Fillers	4	0.0
S	2005	59	Paints, laquers and varnishes	3	0.0
FIN	2005	34	Laboratory chemicals		
FIN	2005	41	Pharmaceuticals		
FIN	2005	48	Solvents		
FIN	2005	50	Surface-active agents		
FIN	2005	55	Others		
FIN	2005	59	Paints, laquers and varnishes		
FIN	2005	09	Cleaning/washing agents		

*The information "0.0 tons" means that the volume is less than 100 kg for that particular branch of industry.
**The reason for the lack of information on the number of preparations and tons particularly for Finland is that data are kept confidential if the substance is a component in less than 4 preparations.

In 2008, the following use categories (UC62) for 2-ethoxyethanol have been notified in the SPIN database: Paints, laquers and varnishes, adhesives, binding agents, laboratory chemicals, pharmaceuticals, others.

Use restrictions

EGEE is listed in Annex XVII, Group 30, of the REACH regulation[7] and shall not be placed on the market, or used for supply to the general public. Suppliers shall ensure before the placing on the market that the packaging of such substances and mixtures is marked visibly, legibly and indelibly as follows: "Restricted to professional users".

According to the Cosmetics Directive 76/768/EEC[8], Annex II, No. 666, 2-ethoxyethanol must not form part of the composition of cosmetic products.

Due to its boiling point of 135 – 137 °C at 1013hPa EGEE falls under the definition as VOC according to Directive 2004/42/EC[9] on the limitation of emissions of volatile organic compounds due to the use of organic solvents in certain paints and varnishes and vehicle refinishing products.

7 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

8 Council Directive 76/768/EEC of 27 July 1976 on the approximation of the laws of the Member States relating to cosmetic products

9 Directive 2004/42/EC of the European Parliament and of the Council of 21 April 2004 on the limitation of emissions of volatile organic compounds due to the use of organic solvents in certain paints and varnishes and vehicle refinishing products and amending Directive 1999/13/EC

An occupational exposure limit value for 2-ethoxyethanol according to Directive 98/24/EEC[10] has been established at community level with the implementation of Commission Directive 2009/161/EU[11] of 17 December 2009 establishing a third list of indicative occupational exposure limit values.

Conclusion on uses

The main proportion (80 %) of EGEE is processed to intermediates such as the 2-ethoxyethanol tert-butyl ether (1-Ethoxy-2-tert-butoxyethane) in chemical industry. The smaller part (20 %) is used as industrial solvent. Previously the substance was widely used in open systems, such as paints for private use, in surface treatment of metals and in repair industry. Besides the industrial use as intermediate and solvent, EGEE was used for the formulation of paints, lacquers, varnishes and printing inks. According to industry there is no remaining wide dispersive use of EGEE outside the chemical industry.

1.3 Information on exposure

Due to its classification, EGEE is banned for public use, major concerns are connected with worker´s exposure due to its reprotoxic properties.

1.3.1 Environment (from EU RAR draft, 2008)

2-Ethoxyethanol is classified as readily biodegradable, and will be rapidly degraded in the air. EGEE is considered as moderate volatile; therefore the extent of volatilization from surface waters can be neglected. Concerning adsorption to soil and sediment using the classification schema by Blume and Ahlsdorf (1993) the adsorption of 2-ethoxyethanol was classified as very low. The measured log Pow of -0.43 does not indicate a relevant bioaccumulation potential; however tests on bioaccumulation are not available according to EU RAR draft, 2008.

The hydrosphere is the target compartment for 2-ethoxyethanol regarding distribution in the environment.

1.3.1.1 Local Exposure

Aquatic compartment:

Exposure data from INEOS, the former 2-ethoxyethanol producing company in Europe, were used to predict environmental concentrations of 2-ethoxyethanol in surface water. INEOS ceased production in 2007; therefore the production scenario is not further considered in this dossier.

10 Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC)

11 Commission Directive 2009/161/EU of 17 December 2009 establishing a third list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC and amending Commission Directive 2000/39/EC

During processing into solvents and intermediates a $\mathbf{C_{local\ water}}$ of 15.8 µg/l for the use as solvent and 25.2 µg/l for the use as intermediate was calculated applying a generic approach.

Atmosphere:

During processing into solvents and intermediates a $\mathbf{C_{local\ air}}$ 6.9 µg/m^3 for the use as solvent and 11 µg/m^3 for the use as intermediate was calculated applying the SIMPLETREAT model (EU RAR draft, 2008).

Terrestrial compartment:

Due to the lack of measured data concentrations in soil were calculated using the SIMPLETREAT model. It was assumed that the main pathway of exposure is via deposition from the atmosphere. A $\mathbf{PEC_{localsoil\text{-}porew}}$ of 1.5µg/l and a $\mathbf{C_{localsoil}}$ of 0.34 µg/kg was calculated.

The calculation of risk for secondary poisoning was assumed to be not necessary due to the lack of bioaccumulation potential (EU RAR draft, 2008).

1.3.1.2 Regional Exposure

Environmental releases of 2-ethoxyethanol to waste water treatment plants (sum of production, intermediate and solvent in chemical industry) were calculated to be 25,75 tons per year, the release into the atmosphere with 10.01 tons per year. Individual releases using the continental EU standard model was calculated to be 0.301 kg/day to air and 65.1 kg/day to waste water treatment plants.

Concerning regional exposure a $\mathbf{C_{regional\ water}}$ of 0.03 µg/l was predicted. For the soil compartment a $\mathbf{C_{regional\ soil}}$ of 3.10^{-4} µg/kg$_{wwt}$ and a $\mathbf{C_{regional\ air}}$ of $5.6.10^{-6}$ mg/m^3 were calculated from the EUSES 2.0.3.

1.3.1.3 Environmental monitoring data

Very few monitoring data of EGEE are available. No environmental monitoring data are included in the EU RAR draft, 2008. Some studies are available from the Hazardous substances data bank. Limited monitoring data are summarised in the Priority Substances List Assessment Report for 2-Ethoxyethanol under the Canadian Environmental Protection Act (Health Canada, 1999).

Environmental Air Concentrations:

In the Windsor Air Quality Study, the concentrations of 2-ethoxyethanol in 7 samples from the city of Windsor (OMEE, 1994 in Health Canada, 1999) were less than the limit of detection (0.81 µg/m^3) in all samples.

2-EEGE was not detected in samples of ambient air collected at six locations in the United States in 1984-1985 (limit of detection 0.25 µg/m^3) (Sheldon et al., 1988 in Health Canada,1999).

Environmental Water Concentrations:

EGEE was detected in the polluted water of the Hayashida River (Japan) in the range of 250-1200 ppb, i..e. 250-1200 µg 2-ethoxyethanol/L (Yasuhara (1981).

1.3.2 Human Exposure

In this chapter data from the EU RAR draft, 2008 are summarized as well as additional exposure data from different countries.

1.3.2.1 General Information

As a result of its adverse reproductive effects 2-ethoxyethanol has been partly replaced by other substances in European countries during the last years. Various products such as consumer goods, household products, cosmetics, pesticide formulations, pharmaceutical preparations and medicines, photo-resist mixtures for semiconductor fabrication and applications with poorly controlled exposure should not contain EGEE any longer. According to information from industry EGEE is no longer used in printing inks or in the manufacturing of electronic components, following the exclusion of EGEE from production and distribution of printing inks from the European Technical Committee “printing inks”.

The decline in use can be demonstrated by the decrease in production volume from 1360 tons in 2002 to 100 tons in 2006. Production in Europe has been ceased in 2007.

However, the area of concern has been occupational exposure to EGEE, which is still used as intermediate and solvent in European industries and by commercial users.

1.3.2.2 Occupational Exposure

Exposure ranges depend on the particular operation conditions and the risk reduction measures in use.

Within the EU different Occupational exposure limits (OEL) exist, the lowest applied in Finland with 7.5 mg/m^3, in most countries in the range of 18- 19 mg/m^3, in some cases markedly higher: such as almost 2-fold (37 mg/m^3) in UK and 4-fold (74 mg/m^3) in Greece.

Table 12: Occupational exposure limits (OEL) and short term exposure levels (STEL) applied in the EU

Country	OEL (mg/m3)	STEL (mg/m3)
Greece (2001)	74	-
United Kingdom (2005)	37	-
France (2005)	19	-
Germany (2006), Switzerland (2005)	19*	152
Austria (2006)	19	76
Sweden (2005)	19	40
The Netherlands (2006)	19	38
Denmark (2005), Iceland (2001)	18.5	-
Belgium (2002), Norway (2003), Ireland (2002), Portugal (2004), Spain (2006), Italy (2006), USA (ACGIH) (2006)	18	-
Finland (2005)	7.5	-

(Ariel, 2000 in EU RAR draft, 2008)*Remark “Z”: This OEL does not exclude the risk of developmental toxicity

In Poland for 2-ethoxyethanol a standard OEL (8h) of 20 mg/m^3 is currently set and a short-term OEL (15 minutes) of 80 mg/m^3. However it is planned to set a new standard OEL (8h) of 5 mg/m^3.

An indicative occupational exposure limit value for 2-ethoxyethanol has been established at community level according to Directive 98/24/EEC implemented by Commission Directive 2009/161/EU of 17 December 2009 establishing a third list of indicative occupational exposure limit values (Table 13).

According to the Recommendation from the Scientific Committee on Occupational Exposure Limits (SCOEL)[12] the critical effects of 2-ethoxyethanol and 2-ethoxyethyl acetate are on reproduction and the blood, which are detected in experimental animals and in humans. As humans are regarded more sensitive than animals, only human studies (even if they are of limited validity) were used for deriving an OEL: For effects in humans on haematopoesis, effect levels of 2.6 ppm (maximum 21.5 ppm; Welch and Cullen 1988) and 3.0 ppm (maximum 18.3 ppm) and a level of no significant effects of 1.8 ppm (maximum 8.1 ppm) (Kim et al. 1999) were derived. If dermal absorption is avoided, an 8-h TWA of 2 ppm should protect from effects on haematopoesis and fertility. The TWA will prevent from developmental toxicity (NOAEL 50 ppm), provided that dermal exposure is avoided and the biological limit value is observed. Sufficient data were not available to recommend a STEL (ACGIH 2001 a, b). A "skin" notation is recommended as dermal absorption can contribute substantially to the total body burden.

[12] SCOEL/SUM/116. August 2007 -- *Recommendation from the Scientific Committee on Occupational Exposure Limits for 2-Ethoxyethanol and 2-Ethoxyethyl acetate*" (http://ec.europa.eu/social/BlobServlet?docId=3871&langId=en)

Table 13: Indicative occupational exposure limit value (IOELV) according to Dir 2009/161/EU

CAS	NAME OF AGENT	LIMIT VALUES				Notation
		8 hours		Short term		
		mg/m ^{3}	ppm	mg/m ^{3}	ppm	
110-80-5	2-ethoxyethanol	8	2	-	-	skin

2-Ethoxyethanol is well absorbed via the respiratory tract, the skin and the gastrointestinal tract. High absorption percentages for different routes of exposure are assumed.

Especially inhalation and dermal exposure is expected for workers. Occupational exposure and internal body burden was calculated in the EU RAR draft, 2008. Within the EU RAR draft, 2008 only the production and the further processing as an intermediate was considered.

Inhalation exposure is based on measured exposure levels (after 1990) from which - if possible 95th percentile were derived, representing worst case situations.

Concerning dermal exposure it was differentiated if potential dermal exposure occurs (estimate of substance landing outside of work wear and on the exposed skin) and actual dermal exposure (estimate of the amount of a substance actually reaching the skin).

Within the EU RAR draft, 2008 the scenario of production and further processing of 2-ethoxyethanol in the large-scale chemical industry was considered assuming that EGEE is used in closed systems. Exposure occurs if the systems are breached for certain activities, e.g. drumming.

Due to the information that suitable gloves (tested according to EN 374) are used regularly dermal exposure during production and further processing was calculated using the EASE model assuming a protection efficiency of 90 %. Table 14 gives an overview on exposure conditions at production and further processing as an intermediate.

Table 14: Occupational exposure assessment (EU RAR draft, 2008)

Inhalation exposure (RWC)								
Scenario number, Area of production and use	**Form of exposure**	**Activity**	**Duration [h/day]**	**Frequency [days/year]**	**Shift average concentration [mg/m3]**	**Method**	**Short-term concentration [mg/m3]**	**Method**
Production and further processing as an intermediate	vapour (liquid)	drumming, loading, cleaning, maintenance	shift length (assumed)	10-15 (one campaign)	3	95th percentile	-	-
Dermal exposure (RWC)								
Scenario number, Area of production and use	**Form of exposure**	**Activity**	**Frequency [days/year]**	**Contact level 1)**	**Level of exposure [mg/cm2/ day]**	**Exposed area [cm2]**	**Shift average [mg/person/ day]**	**Method (use of gloves)**
Production and further processing as an intermediate	liquid	drumming, loading, cleaning, maintenance	10-15 (one campaign)	intermittent	0.1 - 1	210	21	EASE (90 % protection, suitable gloves)

Exposure levels and route specific total internal body burdens were summarised in Table 15.

Table 15: Occupational exposure levels and internal EGEE body burden (EU RAR draft, 2008)

Exposure scenario	**Inhalation shift average**	**Dermal contact shift average**		**Internal body burden of workers after repeated exposure**		
				Inhalation(1)	**Dermal(2)**	**Combined**
	mg/m3	mg/p/d	mg/kg/d	mg/kg/d		
1. Production and further processing as an intermediate	3	21(3)	0.3	0.27	0.15	0.42

(1) based on the assumption of 64% inhalative absorption; breathing volume of 10 m^3 per shift
(2) based on the assumption of 50% systemic availability of 2-ethoxyethanol after dermal contact
(3) EASE (90 % protection by suitable gloves)

Workplace Exposure Data

Austria:

Workplace exposure data exist from two sampling campaigns in Austrian workplaces.

Table 16: Austrian Workplace Exposure data

Glycol ether	CAS-No.	No. of measure-ments	No. of MAK-exceedances (%)	Work place/scenario	Max.	Date	Data obtained from
EGEE	110-80-5	2	-	Spray painting	18 mg/m^3	1996/97	Labour inspectorate
EGEE	110-80-5	1	-	Retouch	4 mg/m^3	1996/97	Labour inspectorate
EGEE	110-80-5	28	19 (67,9%)	Printer shops	30,5 ppm	2006/2007	AUVA

"MAK": Maximale Arbeitsplatzkonzentration: OELV: 19mg/m^3 (5 ppm); STEL: 76 mg/m^3 (20 ppm). AUVA: Austrian Social Insurance for Occupational Risks.

Measuring-campaigns at workplaces were performed in Austria in 1996/1997 and in 2006/2007 by the Labour Inspectorate and the Austrian Social Insurance for Occupational Risks (AUVA).

Up to 6-fold OEL value exceedances were reported in 2006/2007 measured in printer shops. From 28 measurements performed 19 (i.e. 67%) exceeded the OEL. Values ranged from below detection limit to 30.5 ppm.

France:

A comprehensive investigation of exposure to glycol ethers has been published in the AFSSET report (2008).

Table 17: Exposure Measurements conducted between 1987 and 1998

			Exposure concentration (mg/m³)			
Glycol ether	CAS-No.	No. of measurements with professional exposure to EGEE	mean	median	95-percentil	maximum
EGEE	110-80-5	347	3,1	0,5	13	53,6

Measurement period between 60 and 480 minutes. Information extracted from the COLCHIC database from INRS, 1999

Table 18: Exposure Measurements conducted between 2000 and 2006

			Exposure concentration (mg/m³)			
Glycol ether	CAS-No.	No. of measurements with professional exposure to EGEE	mean	median	95-percentil	maximum
EGEE	110-80-5	60	8,94	8,69	21,00	27,40

Measurement period between 60 and 480 minutes. Information extracted from the COLCHIC database from INRS, 1999

These data show that overall exposure concentrations declined from the period 1987- 1998 to the period 2000 – 2006. Whereas mean and median concentrations increased (3.1 mg/m^3 and 0.5 mg/m^3 to 8.94 mg/m^3 and 8.69 mg/m^3 respectively), maximum concentrations declined (53.6 mg/m^{3}to 27.40 mg/m^3).

Germany

Exposure Database MEGA

Within the period 2000 - 2009 290 EGEE measurements in 427 workplaces were performed in Germany by the Institute for Occupational Safety and Health of the German Social Accident Insurance (IFA).

Data were derived from the Exposure Database MEGA (Measurement data relating to workplace exposure to hazardous substances). 98.9% of the data from personal sampling measurements in 90 workplaces were below the detection limit of 6.7 mg/m^3; measurements from stationary sampling procedures were in 99.1% below the detection limit of 4.4 mg/m^3.

Table 19: EGEE Exposure data from MEGA

Glycol ether	**CAS-No.**	**No. of measurements**	**personal exposure (pe) or stationary analyses (sa)**	**No. of workplaces**	**LOD Limit of detection (mg/m^3)**	**No. meas. below LOD (%)**
EGEE	110-80-5	70	pe	95	6.7	94 (98.9)
EGEE	110-80-5	347	sa	219	4.4	339 (99.1)

The measurements have been performed most frequently in the following industrial sectors: electro technology, metal and wood processing, plastic production and processing, paint finishing, printing and office.

Conclusion: Monitoring data from European countries indicate declining concentrations in various workplaces, due to substitution and restrictions. However, exceedance of OELVs was reported for Austria and France in several cases.

1.3.2.3 Consumer Exposure

Consumer Products

Data from 1995 indicate that consumers had been exposed to 2-ethoxyethanol from different sources. For example a European patent application for hair dye lists a concentration of 2-ethoxyethanol of 12% (Cotteret, 1995).

According to the 1993 Products Register in Sweden (reporting of the composition of products manufactured or imported in Sweden is mandatory), 2-ethoxyethanol and its acetate were ingredients in 137 and 170 products, totalling 105-242 and 172-270 tonnes/year, respectively, of pure substance (Johanson and Rick, 1996).

Monitoring data from consumer products were also reported in AFSSET (2008); 14 carpets were analysed and EGEE emissions were detected from two carpets : (Day3: 8.3µg/m^3 and <LOD 2µg/m^3, Day28: 130 and 60µg/m^3) (UFC Que Choisir, N°425, April 2005).

EGEE has been detected on surfaces of Danish toys, measured within a measurement programme of the Danish EPA. In 2 out of 15 toys concentrations of 2 and 17 µg/cm^2 EGEE was detected, resulting in an oral uptake of 0.55 and 5.4 µg/kg respectively (Hansen & Pedersen, 2005).

Data from the US show that concentrations of 2-ethoxyethanol of up to 5% were reported in various consumer products, including hard surface cleaners and windshield washing fluid (Flick, 1986). In following investigations of "advanced" cleaning product formulations, none of the products contained 2-ethoxyethanol or 2-ethoxyethyl acetate (Flick, 1994).

Table 20: Emissions of 2-ethoxyethanol and its acetate from consumer products in the US

(CARB 1991 in Health Canada, 1999)*

Product category	Number of products with detectable emissions	Amount emitted (µg/g product) Glycol ether
Adhesives	3 (as 2-ethoxyethanol) 5 (as 2-ethoxyethyl acetate)	0.1-200 0.1-900
Coatings	14 (as 2-ethoxyethanol) 66 (as 2-ethoxyethyl acetate)	0.09-450 0.05-1578
Fabric	1 (as 2-ethoxyethanol) 3 (as 2-ethoxyethyl acetate)	0.23 0.07-0.7
Pens / inks	6 (as 2-ethoxyethanol) 5 (as 2-ethoxyethyl acetate)	0.1-2800 0.49-4.3
Foam / plastic products	2 (as 2-ethoxyethyl acetate)	0.095-0.7

*according to CARB, 1991 data should be considered as qualitative due to elevated temperature and closed chamber conditions

Consumer use of EGEE is regulated in the EU by several regulations such as Annex XVII, Group 30 of the REACH-Regulation, Annex II of the Cosmetics Directive, or the VOC Directive (see also « Use restrictions » in Chapter 1.2)

According to the EU RAR draft, 2008 a risk assessment for consumers does not have to be performed because no exposure through consumer products is expected.

Monitoring Data

Indoor Air Concentrations

Few data are available concerning indoor air concentrations of EGEE. In northern Italy, six indoor air samples collected from homes in 1983-1984 contained 2-ethoxyethanol concentrations of up to 60 µg/m^3 (De Bortoli et al., 1986 in Health Canada 1999). 2-Ethoxyethanol was detected at concentrations of up to 18.3 µg/m^3 in indoor air samples collected in new buildings (hospital, office, nursing home) in the United States. In older buildings (office, nursing home, school), concentrations were lower (i.e., up to 4.15 µg/m^3) (Sheldon et al., 1988).

France

During the campaign Habit'Air Nord-Pas-de-Calais, which was carried out between February and August 2005, glycol ethers have been investigated. Passive sampling was performed over a week in 60 main residences, which were recruited on voluntary basis. The median of the total of the measured glycol ethers was less than 2 µg/m³. The maxima were between 4 µg/m³ (EGEE) and 20 µg/m³ (1-methoxy-2-propanol, PGME). (AFSSET, 2008).

Table 21: Concentration of EGEE (µg/m³) in 60 residences in the North of Pas-de-Calais (Feb. to August 2005)

Glycol ether	Median	Minimum	Maximum
EGEE	<2.0	<2.0	4.0

Stationary analysis during 1 week

Complementary measurements have been performed by *L'Ecole des Mines de Douai* in the same housings:

Table 22: Concentration of EGEE (µg/m³) in 60 residences in the North of Pas-de-Calais (Feb. to August 2005)

Glycol ether	Limit of detection	Frequency of detection	Median	Maximum
EGEE	0,02	7%	1.0	2.6

1.3.2.4 Indirect exposure via the environment

In order to determine indirect exposure of man to 2-ethoxyethanol via the environment, emissions of the most significant point source (industrial use as intermediate and solvent) to food, drinking water and air were used for the calculation of the possible maximum intake (worst case). Furthermore the percentage of total uptake for EGEE was calculated (see Table 23).

Table 23: Calculated uptake quantities result

Uptake route	% of total uptake for 2-ethoxyethanol	
	local	regional
drinking water	5.95	98.22
fish	0.03	0.49
plant shoot	74.16	0.51
root	0.29	0.65
meat	< 0.01	< 0.01
milk	0.02	0.01
air	19.55	0.48

According to the EU RAR draft, 2008 plant shoot is the most relevant source of EGEE for the local exposure scenario, whereas it is drinking water for the regional exposure.

2 CURRENT KNOWLEDGE ON ALTERNATIVES

2.1 Alternative substances

According to the German Technical Rules for Hazardous Substances TRGS 609 (TRGS 609, 1992)[13] the use of alternative substances as a solvent in lacquer and plastic industry has to be investigated in detail for each application. Therefore it is not possible to list alternative substances for all applications in general. 1-methoxy-2-propanol (PGME), 1-methoxy-2-propyl acetate (PGMEA), 2-butoxyethanol (EGBE), 2-butoxyethyl acetate (EGBEA), and ethyl-3-ethoxypropionate (EEP) were mentioned as possible substitutes for methoxyethanol, ethoxyethanol and their acetates. According to TRGS 609 these substances may be used as alternatives regarding their toxicological properties. None of them are classified as CMR, with PGME, PGMEA, EGBE and EGBEA included in Annex VI of the CLP Regulation and EEP with no harmonised classification (see Table 24). Information on alternative substances for other applications was not available in this paper.

According to US Occupational Safety and Health Administration (OSHA, 1993) the most common substitutes for 2-methoxyethanol, 2-ethoxyethanol and their acetates are PGME, EGBE, ethylene glycol monopropyl ether (EGPE) and their acetates (PGMEA, EGBEA, EGPEA). These chemicals account for almost 90 percent of reported substitutions.

According to OSHA (2003) use of 2-methoxyethanol, 2-ethoxyethanol and their acetates has largely been replaced by less-toxic substitutes, primarily by ethylene glycol butyl ethers from

[13] TRGS 609 (1992). Technical Rules for Hazardous Substances. *Federal Institute for Occupational Safety and Health*. In German: Technische Regeln für Gefahrstoffe, Ersatzstoffe, Ersatzverfahren und Verwendungsbeschränkungen für Methyl- und Ethylglykol sowie deren Acetate

the E-series (The E-series, the ethylene glycol ethers, consist mainly of ethylene glycol methyl, ethyl and butyl ethers), P-series glycol ethers (propylene glycol ethers), and ethyl-3-ethoxypropionate.

Table 24: List of harmonised classification and labelling of alternative substances.

Abbreviation	Chemical Name(s)	CAS-Number	EC-Number	Classification**		Labelling	
				Hazard Class and Category Code(s)	Hazard Statement Code(s)	Pictogram Signal Word Code(s)	Hazard Statement Code(s)
PGME	propylene glycol methyl ether; 1-methoxy-2-propanol	107-98-2	203-539-1	Flam. Liq. 3 STOT SE 3	H226 H336	GHS02 GHS07 Wng	H226 H336
PGMEA	Propylene glycol methyl ether acetate; 2-methoxy-1-methylethyl acetate; 1-methoxy-2-propyl acetate	108-65-6	203-603-9	Flam. Liq. 3	H226	GHS02 Wng	H226
EGBE	Ethylene glycol butyl ether; 2-butoxyethanol; butyl cellosolve	111-76-2	203-905-0	Acute Tox. 4 * Acute Tox. 4 * Acute Tox. 4 * Eye Irrit. 2 Skin Irrit. 2	H332 H312 H302 H319 H315	GHS07 Wng	H332 H312 H302 H319 H315
EGBEA	Ethylene glycol butyl ether acetate; 2-butoxyethyl acetate; butyl glycol acetate	112-07-2	203-933-3	Acute Tox. 4 * Acute Tox. 4 *	H332 H312	GHS07 Wng	H332 H312
EGPE	Ethylene glycol propyl ether; Ethylene glycol monopropyl ether; 2-(propyloxy)ethanol	2807-30-9	220-548-6	Acute Tox. 4 * Eye Irrit. 2	H312 H319	GHS07 Wng	H312 H319
EGPEA	Ethylene glycol propyl ether	20706-25-6	-				

	acetate; Ethylene glycol monopropyl ether acetate; 2-propoxyethyl acetate; 2-(propyloxy)ethanol acetate			Not classified acc. to CLP Reg
EEP	Ethyl-3-ethoxypropionate	763-69-9	212-112-9	Not classified acc. to CLP Reg

** Classification and labelling of PGME, PGMEA, EGBE, EGBEA and EGPE according to CLP Reg 2008

2.1.1 Volumes of alternative substances

Table 25: Production volumes of alternative substances and the number of production sites within the EU

Alternative substance	Production volume in the EU (tonnes/year)	Year	Number of production sites in the EU	Reference
PGME	188 000	2001-2003	5*	EU RAR PGME[14]
PGMEA	78 000	2001-2003	3*	EU RAR PGMEA[15]
EGBE	155 000	2001-2003	5*	EU RAR EGBE[16]
EGBEA	12800	2001-2003	3*	EU RAR EGBEA[17]
EGPE	n.a.**		5	ESIS[18]
EGPEA	n.a.			
EEP	n.a.			

* Production sites exceeding 1000 tonnes/year, **not available

[14] EU RAR PGME 2006: European Union Risk assessment report 1-methoxypropan-2-ol (PGME) Part I – environment; EUR 22474 EN, 2006

EU RAR PGME 2008: European Union Risk assessment report 1-methoxypropan-2-ol (PGME), Final Human Health draft, TRD_AXVREP_RAR_HH_France_PGME.rtf, October 2008

[15] EU RAR PGMEA 2006: European Union Risk assessment report 2-methoxy-1-methylethyl acetate (PGMEA) Part I - environment; EUR 22484 EN, 2006

EU RAR PGMEA 2008 : European Union Risk assessment report 1-methoxypropan-2-ol acetate, Final Human Health draft, TRD_AXVREP_RAR_HH_France_PGMEA.rtf, October 2008

[16] EU RAR EGBE: European Union Risk assessment report 2-butoxyethanol (EGBE) Part I – environment; EUR 22501 EN, 2006; and Part II Human health, final approved version, R408_0808_HH_CLEAN, August 2008

[17] EU RAR EGBEA: European Union Risk assessment report 2-butoxyethyl acetate (EGBEA) Part I – environment; EUR 22475 EN, 2006; and Part II Human Health, final approved version, R409_0808_HH_CLEAN.DOC, August 2008

[18] http://ecb.jrc.ec.europa.eu/esis/

2.1.2 Risk related information on alternative substances

Information on risks arising from the alternative substances mentioned above was extracted mainly from risk assessments performed according to Reg (EEC) 793/93. In the framework of these assessments the following alternative conclusions may be drawn:

Conclusion (i): There is need for further information and/or testing.

Conclusion (ii): There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (iii): There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

2.1.2.1 1-Methoxy-2-propanol (PGME)

Environment (according to EU RAR PGME, 2006)

Conclusion (ii) is applied to all levels of the life cycle of PGME: production, formulation, processing and private use.

Human Health (according to EU RAR PGME, 2008)

Workers

Conclusion (iii) applies to formulation and industrial spraying (coating/painting) for systemic and local toxicity after repeated dermal exposure, to industrial spraying, cleaning (spraying and wiping) and printing (silk screening and flexography) for systemic toxicity after repeated inhalation exposure and to cleaning spraying and wiping (coating/painting) for eye and respiratory tract irritation. For combined exposure, conclusion (iii) applies for formulation, for coating-painting scenarios (industrial spraying), for cleaning (spraying, wiping), for printing (silk screening, flexography).

Conclusion (ii) is reached for the other toxicological endpoints and the other scenarios.

Consumers

Conclusion (iii) applies to eye and respiratory tract irritation for house cleaners scenarios.

Conclusion (ii) is reached for the other toxicological endpoints and the other scenarios

Humans exposed via the environment

Conclusion (ii) applies.

2.1.2.2 2-Methoxy-1-methylethyl acetate (PGMEA)

Environment (according to EU RAR PGMEA 2006)

Conclusion (ii) is applied to all levels of the life cycle of PGMEA: production, formulation, processing and private use.

Human Health (according to EU RAR PGMEA 2008)

Workers

Conclusion (iii) applies for local effects (chronic irritation of the respiratory tract) due to repeated exposure for coating and painting scenario: industrial (spraying and other works) and decorative and for systemic toxicity due to repeated dermal exposure for formulation and industrial spraying scenarios.

Conclusion (ii) applies for the other toxicological endpoints and the other scenarios.

Consumers

Conclusion (iii) applies for eye and respiratory tract irritation for house cleaners scenarios and for repeated dose toxicity (local effects) for aqueous paints and floor varnishes and for house cleaners scenarios.

Conclusion (ii) applies for the other toxicological endpoints and the other scenarios.

Humans exposed via the environment

Conclusion (ii) applies.

2.1.2.3 2-Butoxyethanol (EGBE, according to EU RAR EGBE)

Environment

Conclusion (ii) is applies to all levels of the life cycle of EGBE: production, formulation,

processing and private use.

Human Health

Workers and Consumers

Conclusion (ii) applies to all scenarios and all toxicological end-points

Humans exposed via the environment

Conclusion (ii) applies.

2.1.2.4 2-Butoxyethyl acetate (EGBEA, according to EU RAR EGBEA)

Environment

Conclusion (ii) is applied to all levels of the life cycle of EGBEA: production, formulation, processing and private use.

Human Health

Workers and Consumers

Conclusion (ii) applies for all end points and for all scenarios

Humans exposed via the environment

Conclusion (ii) applies.

2.1.2.5 2-(Propyloxy)ethanol (EGPE)

No risk assessment following Regulation (EEC) No 793/93 on the evaluation and control of the risks of existing substances has been performed for EGPE.

Human Health (hazard assessment according to OECD SIDS)[19]

EGPE (assessed in a group of four mono ethylene glycol ethers) possesses properties indicating a hazard for human health (reversible eye and skin irritation, reversible CNS depression). Hemolysis and associated organ toxicity are noted in rats, mice and rabbits exposed to EGPE. Humans are many-fold less sensitive to these effects and associated organ toxicity.

An increase in the number of fetuses with skeletal variations was noted in offspring of rats exposed to maternally toxic concentrations of EGPE by inhalation (≥ 200 ppm or 966 mg/m3); the derived NOAEL for developmental toxicity was 100 ppm, i.e. 450 mg/m3.

Environment (hazard assessment according to OECD SIDS)

EGPE shows a low hazard profile.

2.1.2.6 2-(Propyloxy)ethanol acetate (EGPEA)

There was no risk assessment performed pursuant Reg. (EEC) No 793/93 and there is no OECD, SIDS publication available. Kasavage and Katz reported developmental effects by EGPEA in rats (Kasavage and Katz, 1984).

2.1.2.7 Ethyl-3-ethoxypropionate (EEP)

There was no risk assessment performed pursuant Reg. (EEC) No 793/93 and there is no OECD, SIDS publication available. According to Boggs, 1989 EEP is a less toxic substitute for ethylene-glycol-ether solvents in positive photoresists.

[19] OECD SIDS, UNEP PUBLICATIONS, Initial Assessment Report for SIAM 19 Monoethylene glycol ethers; http://www.inchem.org/documents/sids/sids/MonoethyleneGlycolEthers.pdf

3 RISK-RELATED INFORMATION

In this chapter information of the EU RAR draft, 2008 is compiled.

3.1 Environmental Risk assessment

3.1.1 Aquatic compartment

Waste Water Treatment Plants

The highest discharge concentration for waste water treatment plants for use as a solvent in chemical industry was calculated to be 0.63 mg/l and for the use as intermediate 1.01 mg/l. Using these data a Clocal effl/PNEC ratio for waste water treatment plants (WWTP) for the use as intermediate was calculated to be 0.0006 for the use as intermediate and 0.0004 for the use as a solvent.

Aquatic environment

Taken the PEC regional water of 0.03 µg/l the $PEC/PNEC_{water}$ ratio was calculated to be 0.008 for the use as intermediate and 0.013 for the use as a solvent.

Sediment

No separate risk consideration for sediment was conducted within the EU RAR draft, 2008, since physic-chemical properties do not suggest relevant distribution into the sediment. Moreover no data concerning the toxicity of 2-EGEE were available.

Conclusion Aquatic compartment:

PEC/PNEC ratios for WWTPs and for the aquatic compartment in general are far below 1; therefore no risk for the aquatic compartment is expected.

Conclusion ii: There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

3.1.2 Atmosphere

No quantitative risk assessment was undertaken within the EU RAR draft, 2008 due to the lack of ecotoxicity tests for this compartment. Anyhow, the substance reveals short half live ($t_{1/2}$ = approx. 25h) and is considered not to be relevant concerning global warming and ozone depletion.

Conclusion ii: There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

3.1.3 Terrestrial compartment

Releases into the terrestrial compartment are expected to be a result of atmospherical deposition. For industrial use as an intermediate the highest deposition rate is expected; a $PEC_{localsoil}$ of 0.34 µg/kg (dw) in soil and 1.5 µg/l in soil pore water were estimated.

Calculated PEC/PNEC ratios for soil and porewater were calculated to be 0.001 (use as an intermediate) indicating no risk for the terrestrial compartment. By comparison of the $PEC_{localporewater}$ with the aquatic PNEC, the PEC/PNEC ratio is <0.01, indicating no risk.

Conclusion ii: There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

3.2 Human Health Risk assessment

The following section compiles the main considerations of the EU RAR draft, 2008 and focuses on the identified risks occurring at the workplace during production and further processing in the large scale industry due to the reproductive toxicity of EGEE.

2-Ethoxyethanol is well absorbed via the respiratory tract, the skin and the gastrointestinal tract. EGEE is metabolized to 2-ethoxyacetic acid (EAA) and ethylene glycol. The half-life for the excretion of 2-ethoxyacetic acid ranged from 21 h (experimentally conditions) to 57 h (work place conditions) for humans, but only 7 to 12.5 h in rats, which has to be taken into consideration for risk assessment purposes. The extent of absorption after oral exposure is assumed to be 100 % as a worst case scenario. Based on experimental data, 50 % dermal absorption and 64 % absorption via the inhalation route was assumed for risk considerations. For animals a lower absorption via inhalation is expected (30%).

Repeated dose toxicity experiments clearly demonstrated that the blood and haematopoietic system and the male reproductive system were the most sensitive organ systems. Effects on the haematopoietic system such as an increase in erythrocytic fragility, anemia, and in some instances, leucopenia were reported. Pathological changes have occasionally been observed in the spleen, bone marrow or thymus. For oral exposure, the NOAEL (rat) was found to be 93 mg/kg bw/day.

Several epidemiological studies concerning occupational exposure in humans demonstrated toxic effects of EGEE on the reproductive capability in men and women. Also an increase of malformations was positively correlated with occupational exposure to glycol ethers and EGEE. These observations are in accordance with numerous animal experiments which demonstrate effects on fertility and developmental toxicity.

A summary and discussion of reproductive toxicity can be found in the Annex to this dossier including a compilation of the derived NOELs from animal experiments (Table 31).

3.2.1 Occupational Risk characterization (from EU RAR draft, 2008)

As outlined above EGEE is well absorbed via oral, dermal and inhalative exposure. Elimination in humans is very slow compared to animals. The occupational exposure values and internal body burden are given in section 1.3.2.2.

Risk characterization in the EU RAR draft, 2008 was performed using a MOS approach. The MOS i.e. margin of safety approach is based on a comparison of the relevant experimental NOAEL with a reference MOS, which is the product of various assessment factors. The MOS concept and derivation of endpoint specific MOS values for the different routes of exposure for EGEE are described in detail in the EU RAR draft, 2008 and in the strategy for limiting the risks. Hence, in this dossier only the relevant (reference) MOS values are presented.

In addition, measured occupational exposure levels which have not been included in the EU RAR draft, 2008 were compared with "critical exposure levels" derived in the RAR (the adjusted toxicological starting point is directly divided by the reference MOS)). The critical exposure level (in mg/m³ or mg/kg/d) may serve as a direct trigger for decisions when compared with the occupational exposure levels. Concern may be expressed for scenarios with occupational exposure levels higher than the relevant "critical exposure level".

Repeated dose toxicity

Table 26 summarises the results of the risk characterization for repeated dose toxicity and the derivation of MOS and critical exposure levels from the EU RAR draft, 2008. Conclusion (ii) is drawn for inhalation, dermal and combined exposure respectively.

Table 26: Risk characterization using the MOS concept for Repeated Dose Toxicity (EU RAR draft, 2008)

	Inhalation			Dermal			Combined		
Starting point for MOS calculation	90 mg/m³			254 mg/kg/day (external dose)			627mg/kg/day (internal dose)		
Reference MOS	25			60			60		
Critical exposure level	.3.6 mg/m³			0.9 mg/kg/day			0.45 mg/kg/day		
	Exposure (mg/m³)	MOS	Conclusion	Exposure (mg/kg/d)	MOS	Conclusion	Internal body burden (mg/kg/d)	MOS	Conclusion
1. Production and further processing in the large-scale industry	3	30	ii	0.3	180	ii	0.42	64	ii

Comparison of measured exposure data with the critical exposure level: Measurements at work places in Austria and France (see chapter 1.3.2.2, Tables 16 to 18) showed that workplace concentrations exceeded the critical exposure level of 3.6 mg/m^3 for inhalation. Due to a relatively high limit of detection of 6,7 mg/m^3 (personal sampling) and 4,4 mg/m^3 (stationary) for data on workplaces from Germany it is not possible to judge whether the critical exposure level was exceeded.

Fertility impairment

Human data indicate a correlation between the exposure to EGEE and subfertility and sperm effects. However workers were exposed to mixtures of substances and quantitative data of a dose response relationship are not described. Thus risk characterisation concerning fertility impairment is based on experimental results.

Table 27 summarises the results of the risk characterization for fertility impairment and the derivation of MOS and critical exposure levels from the EU RAR draft, 2008. Conclusion (ii) is drawn for inhalation, dermal and combined exposure respectively.

Table 27: Risk characterization using the MOS concept for Fertility impairment (EU RAR draft, 2008)

	Inhalation			**Dermal**			**Combined**		
Starting point for MOS calculation	90 mg/m^3			54 mg/kg/day			27 mg/kg/day		
Reference MOS	12.5			30			30		
Critical exposure level	7.2 mg/m^3			1.8 mg/m^3/day			0.9 mg/kg/day		
	Exposure (mg/m^3)	MOS	Conclusion	Exposure (mg/m^3)	MOS	Conclusion	Exposure (mg/m^3)	MOS	Conclusion
Production and further processing in the large-scale industry	3	30	Ii	0,3	180	Ii	0,42	64	ii

Comparison of measured exposure data with the critical exposure level: Measurements at work places in Austria and France (see chapter 1.3.2.2, Tables 16 to 18) showed that workplace concentrations exceeded the critical exposure level of 7.2 mg/m^3 for inhalation in several cases.

Developmental Toxicity

Human data are available that describe a correlation between spontaneous abortion and exposure to EGEE. However women were exposed to mixtures of substances and quantitative data of a dose response relationship are not described. Thus quantitative risk assessment is based on animal data.

Animal data show embryotoxic and teratogenic effects in several species via different route of application. Developmental effects were induced already at dose levels without obvious maternally toxic effects, respectively borderline effects.

Table 28 summarises the results of the risk characterization for developmental toxicity and the derivation of MOS and critical exposure levels from the EU RAR draft, 2008. Conclusion (iii) is drawn for inhalation, dermal and combined exposure respectively, indicating that there is a need for limiting the risks.

In the EU RAR draft, 2008 an exposure value of 3 mg/m^3 for inhalation was calculated. It is more than four times higher than the corresponding critical exposure level of 0.72 mg/m^3. For dermal exposure the calculated exposure of 0.3 mg/kg/day is almost two times above the critical exposure level of 0.18 mg/kg/day.

The critical exposure level for combined exposure was calculated to be 0.09 mg/kg/day being considerably lower than the internal body burden of 0.42 mg/kg/day.

Comparison of measured exposure data with the critical exposure level: Measurements at work places in Austria and France (see chapter 1.3.2.2, Tables 16 to 18) were found to be markedly higher than the calculated exposure of 3 mg/m^3, which already exceeds the critical exposure level for developmental toxicity (0.72 mg/m^3).

Table 28: Risk characterization using the MOS concept for Developmental Toxicity (EU RAR draft, 2008)

	Inhalation			Dermal			Combined		
Starting point for MOS calculation	9 mg/m³			9 mg/kg/day			4.5 mg/kg/day		
Reference MOS	12.5			50			50		
Critical exposure level	0.72 mg/m³			0.18 mg/kg/day			0.09 mg/kg/day		
	Exposure (mg/m^3)	MOS	Conclusion	Exposure (mg/kg/d)	MOS	Conclusion	Internal body burden (mg/kg/d)	MOS	Conclusion
1. Production and further processing in the large-scale industry	3	3	iii	0.3	30	iii	0.42	10.7	iii[(1)]

[(1)]conclusion iii already results from inhalation and dermal exposure, therefore no specific concern for combined exposure is indicated

3.2.2 Summary of occupational risk assessment

The EU Risk assessment (EU RAR draft, 2008) shows that the workplace exposure of EGEE represents the major area of concern due to its developmental toxicity. The corresponding critical exposure level of 0.72 mg/m3 for inhalation resp. 0.18 mg/kg/day for dermal contact are threefold lower than the exposure values of scenario "production and further processing in the large scale industry" for inhalation (3 mg/m^3) and dermal contact (0.3 mg/kg/day) (see Tables 29 and 30).

The risk reduction strategy of the transitional dossier (EU RRS draft, 2008) recommends to establish at community level occupational exposure limit values for 2-ethoxyethanol according to Directive 98/24/EEC[20], which in the meantime has been implemented by Commission Directive 2009/161/EU[21]. This IOELV for EGEE is however higher than the critical exposure levels elaborated in the EU RAR draft, 2008. Even though the use and, consequently, exposure of EGEE has significantly decreased during the last years (mainly due to substitution measures by industry), the available monitoring data at workplace show that measurable concentrations of EGEE can still be found in certain areas of use (e.g. in printer shops) and that measurable exposure still occurs, which in several cases exceeded both the

20 Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC)

21 Commission Directive 2009/161/EU of 17 December 2009 establishing a third list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC and amending Commission Directive 2000/39/EC

critical exposure levels and the IOELV. These findings clearly support the need for additional risk management measures as are proposed in the present dossier, aiming at a progressive substitution of the substance by non-SVHC alternatives.

Table 29: Ranking of health risks for workers (inhalation), EU RAR draft, 2008

Exposure scenario	Exposure level in mg/m³	Developmental toxicity	Repeated dose toxicity, systemic	Acute toxicity	Fertility
		Critical exposure level in mg/m³			
		0.72	3.6	7.2	7.2
1. Production and further processing in the large scale industry	3	iii	ii	ii	ii

Table 30: Ranking of health risks for workers (dermal contact), EU RAR draft, 2008

Exposure scenario	Exposure level in mg/kg/day	Developmental toxicity	Repeated dose toxicity, systemic	Acute toxicity	Fertility
		Critical exposure level in mg/kg/day			
		0.18	0.9	1.1	1.8
1. Production and further processing in the large scale industry	0.3	iii	ii	ii	ii

3.2.3 Consumers

According to the EU RAR draft, 2008 there is no evidence for direct exposure of consumers to 2-ethoxyethanol and therefore no risk is expected.

According to Cicolella *et* al., 2006 glycol ethers, including EGEE, were used for painting at concentrations of 0.9% and above. In order to find out whether consumers using paints containing EGEE at the concentration limit of 0.5% were at risk, an exposure assessment was performed assuming an EGEE conentration of 0.5% in paints (see below).

Estimation of exposure resulting from the application of consumer products containing 0.5% EGEE

Inhalation exposure

Reasonable worst-case assumption: Inhalation of saturated air:

The saturation concentration of 2-ethoxyethanol in air is estimated from following equation (ideal gas law):

$W = (1000*P*V*M) / (R*T)$

where W is the concentration in air (mg/m^3)

P is the vapour pressure (530 Pa at 25°C) (Kirk-Othmer, 1980)

V is the volume of air (1 m^3)

M is the molecular weight (90.1 g/mol)

R is the gas constant (8.314 J/mol/K)

T is the temperature (293 K ~ 25°C)

Tier 1: Using the values listed above, the saturation concentration of 2-ethoxyethanol in air is calculated to be 19603 mg/m^3. Assuming that 2-ethoxyethanol is saturated in air due to gaseous release as a conservative assumption, an inhalation rate of 1.25 m^3/h, an inhalation absorption of 100% and a duration of exposure of 8 hours, results in a systemic exposure level of 196030 mg 2-ethoxyethanol/d. Considering a bodyweight of 60 kg (default, adult), results in 3267 mg/kg bw/d.

19603 mg/m^3 x 1.25 m^3/h x 8h/d x 1 / 60 kg = 3267 mg/kg bw/d

Scenario: Application of 2-ethoxyethanol for painting

1. **Inhalation exposure: Assumption of total release**

The calculation of the 2-ethoxyethanol concentration in air is based on the following assumptions.

Applied amount of product: 400 g (estimate of the assessor)

Concentration of 2-ethoxyethanol in product: 0.5% w/w

Room volume: 58 m^3 (default, ConsExpo 4.1)

Referring to the values given above, this results in a concentration of 34.48 mg/m^3 in air

400 g x 0.005 x 1000 (conversion g to mg) / 58 m^3 =34.48 mg/m^3

Tier 1: Assuming the derived concentration of 2-ethoxyethanol in air, an inhalation rate of 1.25 m^3/h, an inhalation absorption of 100% and a duration of 8h exposure, results in a systemic exposure level of 17.2 mg 2-ethoxyethanol/d. Considering a bodyweight of 60 kg, results in 5.747 mg/kg bw/d.

1.72 mg/m^3 x 1.25 m^3/h x 8h/d x 1 /60 kg= 5.747 mg/kg bw/d

2. Dermal exposure: Exposure of both hands

Tier 1: Assuming one event per day of dermal exposure of both hands (840 cm^2, default, surface area of both hands of an adult), a thickness of 0.01 cm of film on skin (thin layer model), a concentration of 0.5 % w/w present in product (density: 1000 mg/cm^3; default, density of pure water) and a dermal absorption of 100%, results in a systemic exposure level of 42 mg/d via the dermal route. Considering a bodyweight of 60 kg, results in 0.700 mg/kg bw/d.

1 x 840 cm^2 x 0.001 cm x 1000 mg/cm^3 x 0.005 x 1 /60 kg = 0.700 mg/kg bw/d

3. Combined exposure

Considering operators are exposed via the inhalation and the dermal route, combination of the first and the second scenario results in 6.447 mg/kg bw/d (5.747 + 0.700).

Scenario: Application of 2-ethoxyethanol for window-cleaning

In order to find out whether consumers using window-cleaning agents containing EGEE at the concentration limit of 0.5 % were at risk, an exposure assessment was performed assuming an EGEE conentration of 0.5 % in window-cleaning agents (see below).

1. Inhalation exposure: Assumption of total release

The calculation of the 2-ethoxyethanol concentration in air is based on the following assumptions.

Applied amount of product: 20 g (estimate of the assessor)

Concentration of 2-ethoxyethanol in product: 0.5% w/w

Room volume: 58 m^3 (default, ConsExpo 4.1; Cleaning and Washing→ All purpose cleaners→ liquid cleaner→ application)

Referring to the values given above, this results in a concentration of 1.72 mg/m^3 in air

20 g x 0.005 x 1000 (conversion g to mg) / 58 m^3 = 1.72 mg/m^3

Tier 1: Assuming the derived concentration of 2-ethoxyethanol in air, an inhalation rate of 1.25 m^3/h, an inhalation absorption of 100% and a duration of 8h exposure, results in a systemic exposure level of 17.2 mg 2-ethoxyethanol/d. Considering a bodyweight of 60 kg, results in 0.287 mg/kg bw/d.

1.72 mg/m^3 x 1.25 m^3/h x 8h/d x 1 /60 kg= 0.287 mg/kg bw/d

2. Dermal exposure: Exposure of both hands

Tier 1: Assuming one event per day of dermal exposure of both hands (840 cm^2, default surface area of both hands of an adult), a thickness of 0.01 cm of film on skin (thin layer model), a concentration of 0.5 % w/w present in product (density: 1000 mg/cm^3; default, density of pure water) and a dermal absorption of 100%, results in a systemic exposure level of 42 mg/d via the dermal route. Considering a bodyweight of 60 kg, results in 0.700 mg/kg bw/d.

1 x 840 cm^2 x 0.001 cm x 1000 mg/cm^3 x 0.005 x 1 /60 kg = 0.700 mg/kg bw/d

3. Combined exposure

Considering operators are exposed via the inhalation and the dermal route, combination of the first and the second scenario result in 0.987 mg/kg bw/d (0.287 + 0.700).

Conclusion:

Two applications (cleaning, painting) for EGEE have been calculated for following consumer products: window-cleaning agent and paint. A theoretical concentration of 0.5% EGEE was assumed to evaluate a potential risk for consumers. Additionally, it is important to note, that all used EGEE from the product will enter the gas-phase, as the substance reveals a high volatility as demonstrated in the reasonable worst case scenario (saturated air) and the applied amounts are expected to release gaseous residues during drying (paints, detergents).

The calculated EGEE-concentration in air for both scenarios are: For window-cleaning a EGEE concentration of 1.72 mg/m^3 and for painting: 34.48 mg/m^3 was calculated. Furthermore, it needs to be stressed that inhalation exposure via spraying of paints and window cleaner was not assessed for these activities (generation of inhalable aerosols). Considering also this source of exposure, the contribution would result in even higher EGEE exposure levels. The dermal exposure would further contribute to total systemic exposure.

Comparing the EGEE concentration (1.72 mg/m^3 and 34.48 mg/m^3) in air from these two scenarios (cleaning, painting) with the critical exposure level[22] for developmental toxicity (0.72 mg/m^3), consumers and professional users were at risk even if the concentration of EGEE was only 0.5 % in window-cleaning agents or paints.

3.2.4 Man exposed indirectly via the environment

The exposure estimations for humans via the environment are summarised in section 1.3.2.3. A total daily intake of 2.67 x 10-3 mg/kg bw/d was calculated for the local scenario. The main contribution is the plant shoot with a fraction of 74 % for oral uptake. The regional exposure of 9.38 x 10-7 mg/kg bw/d via drinking water was considered to be negligible. The NOAEL of 93 mg/kg bw/d for effects on the blood, hematopoietic and male reproductive systems in rats for the oral route from the 13-week study was used for considerations on the margin of safety (MOS). The daily intake was calculated to be 0.00267 mg/kg bw/d. Based on these data conclusion (ii) was derived for this scenario.

[22] The critical exposure level of 0.72 mg/m^3 from the EU RAR 2008 was taken forward for risk characterisation. The critical exposure level is in essence the same as a DNEL: DNEL = NOAEC / product of assessment factors; critical exposure level = NOAEC / reference MOS (see table 29).

Overall conclusion

The EU Risk assessment (2008) shows that the workplace exposure of EGEE represents the major area of concern. The risk reduction strategy of the transitional dossier recommends to establish at community level occupational exposure limit values for 2-ethoxyethanol according to Directive 98/24/EEC, which in the meantime has been implemented by Commission Directive 2009/161/EU. This IOELV for EGEE is however higher than the critical exposure levels elaborated in the EU RAR (2008). Even though the use and, consequently, exposure of EGEE has significantly decreased during the last years (mainly due to substitution measures by industry), the available monitoring data at workplace show that measurable concentrations of EGEE can still be found in certain areas of use (e.g. in printer shops) and that measurable exposure still occurs, which in several cases exceeded both the critical exposure levels and the IOELV. These findings clearly support the need for additional risk management measures as are proposed in the present dossier, aiming at a substitution of EGEE by non-SVHC alternatives.

According to the EU Risk assessment (2008) there is no evidence for direct exposure of consumers to 2-ethoxyethanol and therefore no risk to consumers is expected. However, if consumer exposure to EGEE resulting from two model scenarios (cleaning, painting) is compared to the critical exposure level for developmental toxicity, consumers and professional users would be at risk even if the concentration of EGEE was only 0.5 % in window-cleaning agents or paints.

REFERENCES

Notice:

No re-evaluation was conducted of those references which are cited in this Annex XV SVHC-Dossier and which were taken from the Risk Assessment Report for 2-ethoxyethanol (EU RAR draft, 2008). For the present dossier no comprehensive literature survey was carried out, but focus was given to exposure related data.

2-Ethoxyethanol was prioritised under the Existing Substance Regulation (ESR) (Regulation (EEC) No793/93), however, the risk evaluation and/or risk management work for this substance was not finalised by 1 June 2008 (i.e. the date the ESR regulation was repealed and replaced by the REACH Regulation). As rapporteur of this substance according to the ESR, Germany was required to develop an Annex XV transitional report for this substance. This report contains information on hazard and risk documented in an annexed risk assessment report (RAR) following the structure used under the ESR. It also provides information on what possible actions the submitting Member State considers to be necessary in order to reduce the risks identified in the RAR. The Annex XV transitional report has been submitted to ECHA according to the REACH Regulation (EC) No 1907/2006, Article 136(3).

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ANNEX

Summary and discussion of reproductive toxicity according to EU RAR draft, 2008

Animal data

Several studies in mice and rats demonstrate adverse effects of 2-ethoxyethanol on the male reproductive system via different exposure routes. The effects reported include: reduction of testes weight and testicular atrophy, degeneration of testes, testicular edema, reduction of sperm count and motility, abnormal sperm morphology and spermatocyte degeneration and absence of more mature sperm cells. It is documented that EGEE adversely affected reproductive performance in mice of both sexes for at least one generation. A NOAEL fertility was derived from the study in CD1 mice of Lamb et al. (1984) of 800 mg/kg bw/day whereas it is stated in the EU RAR draft, 2008 that various other studies show spermatoxicity at clearly lower doses.

Male reproductive organ toxicity/spermatoxicity effects were reported in various repeated dose toxicity studies with different species.

It was also clearly shown that 2-ethoxyethanol adversely affects embryonic and fetal development in dose dependent manner. Increasing embryo-/fetomortality, fetal growth retardation and visceral /skeletal malformations and variations were reported at concentrations devoid of maternal toxicity. Table 31 summarises the effects of 2-ethoxyethanol on the reproductive system.

Table 31: Compilation of NOAELs derived from animal studies related to reproductive toxicity

Endpoint	**species**	**NOAEL /NOAEC (route of exposure)**	**study type**	**Reference (in EU RAR draft, 2008)**
Fertility	mouse	800 mg/kg (oral, drinking water)	fertility study exposure in premating period (7 days)	Lamb et al. 1984
Male reproductive organ toxicity	rabbit	100 ppm (390mg/m^3) (inhalatory)	repeated dose toxicity (13 weeks)	Biodynamis Inc 1983, Barbee et al. 1984,
Male reproductive organ toxicity	rat	1250 ppm (109 mg/kg bw/day) (oral)	repeated dose toxicity (13 weeks)	NTP, 1993
Male reproductive organ toxicity	dog	200 µL/kg bw/day (93 mg/kg/d) (oral)	repeated dose toxicity (13 weeks)	Stenger et al. 1971
Developmental Toxicity	rat	10 ppm (39mg/m^3) (inhalatory)	6h/day on g.d.* 6-15, Dev-Tox. study	Doe 1984 b Tinston 1983 a
Developmental Toxicity	rat	23 mg/kg bw (oral)	6h/day on g.d.*1-21 Dev-Tox. Study	Stenger et al. 1971

g.d.: gestational day

Conclusion:

Based on available animal data 2-ethoxyethanol is confirmed as reproductive toxicant and classified and labelled for its effects on fertility and development as Repr. Cat. 2; R 60/R61; and Repr. Cat 1b according to the CLP-Regulation respectively.

Human Data

The possible associations between exposure to glycol ethers and reproductive disorders were first investigated in a case control study (1019 cases, 475 controls) by Veulemans 1993. Exposure to EGEE was assessed by the presence of the urinary metabolites. Ethoxy acetic acid (EAA). EAA was detected in 39 patients and six controls, with a highly significant odds ratio of 3.11 (p=0,004). A high association of the occupational high exposure group with complete azoospermia and severe oligozoospermia was found. The association between urinary EAA and diagnosis remained significant taking into account possible confounders (other industrial spermatotoxic chemicals).

Further studies supported these findings. Table 32 summarises the findings of epidemiological studies on workers exposed to 2-ethoxyethanol.

Table 32: Human studies dealing with occupational exposure to EGEE

Study population	Study design	Effects and findings	Reference (in EU RAR draft, 2008)
Occupational exposure with paint products	Case – Control study (1019 : 475) (infertile vs. fertile) Investigation of metabolite in urine (etoxyacetic acid EAA)	Highly significant assoc. OR: 3.11 (p=0,004), of EAA positive subjects had been occupationally exposed; association with azoospermia and severe oligozoospermia	Veulemans, 1993
73 ship yard painters and 40 controls (non exposed employees)	Cross sectional study, 8-hour time weighted investigation of workplace air (EGEE, EGME)	Proportion of exposed men with oligospermia was 13% versus 5% (controls), proportion of painters with azoospermia was 5% (1% expected) versus 0% OR: 2.8 for oligospermia among non-smoking painters	Welch et al. 1988
Metal casting process workers in Portland, Oregon	Cross sectional study, investigation of workplace air conc. Monitoring EEA in urine 27 exposed: 39 non-exposed	Average sperm count per ejaculate (p.e.) among exposed workers was significantly lower than of controls ($113x10^6$ versus $154x10^6$ p.e.)	Ratcliffe et al.1989

Fabrication room work in silicon-based semiconductor industry (14 US-companies)	Historical and retrospective nation-wide study	Investigation of increased abortion rat and subfertility: Small increase of risk of spontaneous abortion in fab room workers (historical:OR: 1.43, 95% CI: 0.95-2.09); prospective: OR: 1.25, 95% CI: 0.65-1.76); No significant decrease in fertility, but reduced fecundability was suggested for some wifes of fab workers.	Schenker et al. 1995
2 semiconductor plants (eastern USA)	Retrospective cohort study (1980 -1987), 1150 pregnancies (561 female employees, 589 wifes to male)	Investigation of increased abortion rate and subfertility: Higher risk of spontaneous abortion in female workers (OR: 2.8, 95% CI: 1.4-5.6) and subfertility (high exposure group: OR: 4.6, 95% CI:1,6 -13.3) In wifes of male employees nonsignificant increased risk of subfertility in high exposure group was reported: OR: 1.7, 95%CI:0.7-4.3)	Correa et al.1996
Multicenter study in six regions in Europe	Case-Control 984 cases of major congenital malformations and 11134 controls matched for place and date of birth	Risk of congenital malformations related to glycol ether exposure during pregnancy Congenital malformation associated with glycol ether exposure : 1.44, 95%CI:1,10 -1,90 Association appeared particularly strong for neural tube defects, cleft lip and multiple anomalies	Cordier et al. 1997

OR: Odds ratio; CI: Confidence Interval

Conclusion:

Findings from several epidemiological studies indicate an association between occupational exposure to 2-ethoxyethanol (mostly monitored as EAA in urine) and impairment of reproduction in men and women. Whereas in men spermatotoxic effects (azoospermia, oligospermia) were reported, a higher risk in spontaneous abortions was reported in women.

Congenital malformations in humans such as neural tube defects, cleft lip and multiple anomalies were also associated with glycol ether exposure.

According to the EU RAR draft, 2008 the plausibility of the observations from epidemiology is supported by the data of numerous experimental studies, which demonstrated similar effects in laboratory animals.