

Annex XV dossier

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

Substance Name(s): 2-Ethoxyethyl acetate (2-EEA)

EC Number(s): 203-839-2

CAS Number(s): 111-15-9

Submitted by: Belgian Competent Authority
(Belgian Federal Public Service (FPS) Health, Food Chain Safety and
Environment, Risk Management Service)

In cooperation with:
Environment Agency Austria on behalf of the Austrian Competent Authority
(Austrian Federal Ministry of Agriculture, Forestry, Environment and Water
Management)

and
Polish Competent Authority (Bureau for Chemical Substances and
Preparations)

Version: February 2011

CONTENTS

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE AS A CATEGORY 1A OR 1B CMR, PBT, VPVB OR A SUBSTANCE OF AN EQUIVALENT LEVEL OF CONCERN	5
PART I.....	6
JUSTIFICATION	6
1 IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES	6
1.1 Name and other identifiers of the substance	6
1.2 Composition of the substance	7
1.3 Physico-chemical properties.....	8
2 HARMONISED CLASSIFICATION AND LABELLING	9
3 ENVIRONMENTAL FATE PROPERTIES.....	9
4 HUMAN HEALTH HAZARD ASSESSMENT.....	9
4.1 Toxicity for reproduction.....	9
5 ENVIRONMENTAL HAZARD ASSESSMENT	10
6 CONCLUSIONS ON THE SVHC PROPERTIES	10
6.1 PBT, vPvB assessment	10
6.2 CMR assessment.....	10
6.3 Substances of equivalent level of concern assessment.	10
7 OTHER RELEVANT INFORMATION.....	10
PART II	11
INFORMATION ON USE, EXPOSURE, ALTERNATIVES AND RISKS	11
1. INFORMATION ON MANUFACTURE, IMPORT/EXPORT AND USES –CONCLUSIONS ON EXPOSURE	11
1.1. Information on volumes.....	11
1.1.1 Information from Product Register Data (SPIN database).....	12
1.1.2 Information from other Member States	13
1.1.3 Conclusions on volumes	13
1.2 Information on uses	14
1.2.1 EU RAR, 2008.....	14
1.2.2 France	14
1.2.3 Uses according to the SPIN database.....	15
1.2.4 Use restrictions	18
1.2.5 Conclusions on uses.....	19
1.3 Information on exposure.....	19

1.3.1 Human Exposure	19
1.3.1.1 General Information	19
1.3.1.2 Occupational Exposure.....	19
2. CURRENT KNOWLEDGE ON ALTERNATIVES.....	21
3. RISK-RELATED INFORMATION.....	22
3.1 Human Health Risk Assessment	22
REFERENCES	24
ANNEX.....	26

TABLES

Table 1: Substance identity.....	6
Table 2: Constituents	7
Table 3: Impurities.....	7
Table 4: Additives.....	7
Table 5: Overview of physicochemical properties	8
Table 6: Classification according to part 3 of Annex VI, Table 3.1 (list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008	9
Table 7: Classification according to part 3 of Annex VI, Table 3.2 (list of harmonized classification and labelling of hazardous substances from Annex I of Council Directive 67/548/EEC) of Regulation (EC) No 1272/2008.....	9
Table 8: Information on 2-ethoxyethyl acetate tonnages according to pre-registration data	11
Table 9: 2-ethoxyethyl acetate in products according to SPIN for 2005 – 2006.	13
Table 10: 2-ethoxyethyl acetate in products according to SPIN for 2007– 2008.	13
Table 11. Occurrence* of glycol ethers classified as toxic for reproduction (cat. 2) in formulations registered in SEPIA between 2000 and 2006.	15
Table 12: Industrial Uses (NACE) according to the SPIN database (2005-2008).	15
Table 13: Industrial Uses in DK and S (using national codes) according to the SPIN database (2005-2008).....	16
Table 14: Use categories (UC62) according to the SPIN database.....	17
Table 15: Occupational exposure limit values (OEL) applied in different EU countries	20
Table 16: Indicative occupational exposure limit value (IOELV) according to Dir 2009/161/EU.....	20
Table 17: Exposure Measurements conducted between 1987-1998 and between 2000-2006.....	21
Table 18: Exposure Measurements per sector of activity (between 2000 and 2006).....	21
Table 19: Exposure Measurements per workstation (between 2000–2006)	21
Table 20: key studies* considered for the classification of 2-EEA as toxic for reproduction	27

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
COLCHIC	INRS database which contains data on exposure to chemical agents
DGCCRF	Direction Générale de la Concurrence, de la Consommation, et de la Répression des Fraudes

DNEL	Derived No Effect Level
2-EEA	2-Ethoxyethyl acetate (CAS No.111-15-9)
EGEE	2-Ethoxyethanol (CAS No. 110-80-5)
EGME	2-Methoxyethanol (CAS No. 109-86-4)
EuPIA	European Printing Ink Association
EU RAR	European Union Risk Assessment Report
IOELV	Indicative Occupational Exposure Limit Value
INRS	Institut National de Recherche et de Sécurité
IUCLID	International Uniform Chemical Information Database
NACE	Nomenclature générale des Activités économiques dans les Communautés Européennes
NAEL	No Adverse Effect Level
NOAEL	No Observed Adverse Effect Level
OEL	Occupational Exposure Limit
PBT	Persistent, Bioaccumulative and Toxic
1PG2ME	2-Methoxypropanol (isomer beta, CAS No. 1589-47-5)
1PG2MEA	2-Methoxypropyl acetate (isomer beta, CAS No. 70657-70-4)
SCOEL	Scientific Committee on Occupational Exposure Limits
SEPIA	INRS database which contains data on preparations
SPIN	Substances in Preparations in the Nordic countries
STEL	Short Term Exposure Level
SVHC	Substance of Very High Concern
TRGS	Technische Regeln für Gefahrstoffe; Technical rules for Hazardous substances
TWA	Time Weighted Average
vPvB	very Persistent and very Bioaccumulative

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

Substance Name: 2-Ethoxyethyl acetate (2-EEA)

EC Number(s): 203-839-2

CAS number(s): 111-15-9

- 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 1 B¹ which corresponds to classifications as toxic for reproduction category 2².

Summary of how the substance meets the CMR (1A or 1B) criteria

2-ethoxyethyl acetate is listed by index number 607-037-00-7 of Regulation (EC) No 1272/2008 and classified in Annex VI, part 3, Table 3.1 (the list of harmonised classification and labelling of hazardous substances) as toxic for reproduction: Repr. 1B (H360FD: “May damage fertility. May damage the unborn child.”). The corresponding classification in Annex VI, part 3, Table 3.2 (the list of harmonised and classification and labelling of hazardous substances from Annex I to Directive 67/548/EEC) of Regulation (EC) No 1272/2008 is toxic for reproduction, Repr. Cat. 2; R60-61 (“May impair fertility. May cause harm to the unborn child”).

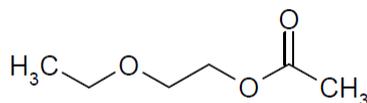
Therefore, this classification of the substance in Regulation (EC) No 1272/2008 shows that the substance meets the criteria for classification as toxic for reproduction in accordance with Article 57 (c) of REACH.

¹ Classification in accordance with Regulation (EC) No 1272/2008 Annex VI, part 3, Table 3.1 List of harmonised classification and labelling of hazardous substances.

² Classification in accordance with Regulation (EC) No 1272/2008, Annex VI, part 3, Table 3.2 List of harmonised classification and labelling of hazardous substances (from Annex I to Council Directive 67/548/EEC).

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:	203-839-2
EC name:	2-Ethoxyethyl acetate
CAS number (in the EC inventory):	111-15-9
CAS number:	111-15-9
CAS name:	Ethanol, 2-ethoxy-, acetate
IUPAC name:	2-Ethoxyethyl acetate
Index number in Annex VI of the CLP Regulation	607-037-00-7
Molecular formula:	C ₆ H ₁₂ O ₃
Molecular weight range:	132.1 g/mol
Synonyms:	Ethylglycol acetate; ethylene glycol mono ethyl ether acetate; 2-EEA; acetic acid, 2-ethoxyethyl ester; ethoxyethanol acetate

Structural formula:

1.2 Composition of the substance

Name: 2-Ethoxyethyl acetate

Description:

Degree of purity: $\geq 99\%$ w/w

Table 2: Constituents

Constituents	Typical concentration	Concentration range	Remarks
2-Ethoxyethyl acetate EC Number: 203-839-2	$\geq 99\%$ w/w		

Table 3: Impurities

Impurities	Typical concentration	Concentration range	Remarks
ethylene di(acetate) EC Number: 203-881-1	< 0.5% w/w		
2-ethoxyethanol EC Number: 203-804-1	< 0.5% w/w		
2-ethoxyethyl formate CAS Number: 66736-44-5	< 0.1% w/w		
Water EC Number: 231-791-2	< 0.1% w/w		
2-hydroxyethyl acetate EC Number: 208-821-8	< 0.05% w/w		
2-(2-ethoxyethoxy)ethyl acetate EC Number: 203-940-1	< 0.01% w/w		

Table 4: Additives

Additives	Typical concentration	Concentration range	Remarks
2,6-di-tert-butyl-p-cresol EC Number: 204-881-4	0.008-0.012%		Function : inhibition of peroxyde formation

1.3 Physico-chemical properties

Table 5: Overview of physicochemical properties

Property	Value	Remarks
Physical state at 20°C and 101.3 kPa	Colourless liquid	
Melting/freezing point	<-62 °C	Kirk-Othmer (1980)
Boiling point	156 °C	Merck-Index (1989)
Vapour pressure	270 Pa at 20°C	Kirk-Othmer (1980)
Water solubility	229g/l at 20°C	Kirk-Othmer (1980)
Partition coefficient n-octanol/water (log value)	Log Pow 0.24 (experimental) ³	Hüls AG (1989)
Flammability	Flammable ⁴	Chemsafe (1996)
Flash point	51°C (closed up),	Chemsafe (1996)
Ignition temperature	380°C (DIN 51794)	Chemsafe (1996)
Explosive properties	not explosive ⁵	Chemsafe (1996)
Oxidizing properties	No oxidizing properties ⁶	Chemsafe (1996)
Henry's law constant	0.16 Pa*m ³ /mol ⁷	

The data included in the tables 1 to 5 were extracted from the Risk Assessment Report for 2-ethoxyethyl acetate (EU RAR, 2008). No re-evaluation of those references was conducted.

³ Determined by shaking method

⁴ Test A.10 not conducted (substance is a liquid)
Test A.12 and A.13 not conducted because of structural reasons

⁵ No test conducted because of structural reasons

⁶ No test conducted because of structural reasons

⁷ The Henry law constant is based on the Water solubility-Vapour Pressure Method. Johanson Dynesius present an experimental Henry law constant as 0.36 Pa m³/mol (Johanson Dynesius: liquid-air partition coefficient of six commonly used glycol ethers. Br J Ind Med 45 (8): 561-564). The value of 0.16 Pa m³/mol corresponds with a calculated value from the EPI database (0.15 Pa m³/mol) based on water solubility and vapour pressure data and is therefore used for the risk assessment.

2 HARMONISED CLASSIFICATION AND LABELLING

Pursuant to the first ATP to Regulation (EC) No 1272/2008 (Commission Regulation (EC) No 790/20095) as of 1 December 2010, 2-ethoxyethyl acetate is covered by index number 607-037-00-7 in Annex VI, part 3 of Reg. (EC) No 1272/2008 as follows:

Table 6: Classification according to part 3 of Annex VI, Table 3.1 (list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008

Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Spec. Conc. Limits, M-factors	Notes
				Hazard Class and Category Code(s)	Hazard statement code(s)	Pictogram, Signal Word Code(s)	Hazard statement code(s)	Suppl. Hazard statement code(s)		
607-037-00-7	2-ethoxyethyl acetate; ethylglycol acetate	203-839-2	111-15-9	Flam. Liq. 3 Repr. 1B Acute Tox. 4 * Acute Tox. 4 * Acute Tox. 4 *	H226 H360FD H332 H312 H302	GHS02 GHS08 GHS07 Dgr	H226 H360FD H332 H312 H302			

Table 7: Classification according to part 3 of Annex VI, Table 3.2 (list of harmonized classification and labelling of hazardous substances from Annex I of Council Directive 67/548/EEC) of Regulation (EC) No 1272/2008

INDEX NO	INTERNATIONAL CHEMICAL IDENTIFICATION	EC NO	CAS NO	CLASSIFICATION	LABELLING	CONCENTRATION LIMITS	NOTES
607-037-00-7	2-ethoxyethyl acetate; ethylglycol acetate	203-839-2	111-15-9	R10 Repr. Cat. 2; R60-61 Xn; R20/21/22	T R: 60-61-10-20/21/22 S: 53-45		

3 ENVIRONMENTAL FATE PROPERTIES

Not relevant for this type of dossier.

4 HUMAN HEALTH HAZARD ASSESSMENT

4.1 Toxicity for reproduction

A summary of reproductive toxicity can be found in the Annex.

5 ENVIRONMENTAL HAZARD ASSESSMENT

Not relevant for this type of dossier.

6 CONCLUSIONS ON THE SVHC PROPERTIES

6.1 PBT, vPvB assessment

Not relevant.

6.2 CMR assessment

2-ethoxyethyl acetate is listed by index number 607-037-00-7 of Regulation (EC) No 1272/2008 and classified in Annex VI, part 3, Table 3.1 (the list of harmonised classification and labelling of hazardous substances) as toxic for reproduction: Repr. 1B (H360FD: “May damage fertility. May damage the unborn child.”). The corresponding classification in Annex VI, part 3, Table 3.2 (the list of harmonised and classification and labelling of hazardous substances from Annex I to Directive 67/548/EEC) of Regulation (EC) No 1272/2008 is toxic for reproduction, Repr. Cat. 2; R60-61 (“May impair fertility. May cause harm to the unborn child”).

Therefore, this classification of the substance 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.

6.3 Substances of equivalent level of concern assessment.

Not relevant.

7 OTHER RELEVANT INFORMATION

Two related substances, 2-Methoxyethanol (EGME) (CAS No. 109-86-4) and 2-Ethoxyethanol (EGEE) (CAS No. 110-80-5) are included in the candidate list of Substances of Very High Concern.

PART II**INFORMATION ON USE, EXPOSURE, ALTERNATIVES AND RISKS****1. INFORMATION ON MANUFACTURE, IMPORT/EXPORT AND USES – CONCLUSIONS ON EXPOSURE****1.1. Information on volumes****Existing Substances Regulation**

2-EEA has been prioritized under the former Existing Substances Regulation program of Reg. (EEC) No 793/93⁸ and a Risk Assessment has been performed by the rapporteur Germany (the Federal Institute for Occupational Safety and Health) and finalized in February 2008 (EU RAR, 2008). The Human Health section of the Risk Assessment Report of 2-Ethoxyethyl acetate has not been carried out.

According to the EU RAR, 2008, six producers /importers were listed in the IUCLID from 1996. The last European production site ceased production in 1996. In August 2002 the last known importer announced that it discontinued all sales of 2-EEA. According to industry, estimated sales in the year 2000 were less than 5000 tonnes. With the withdrawal from the market it was predicted *“that the amount of product onto the EU market may rapidly drop even below 1000 tonnes per year in the near future”*.

Pre-registration data

An excerpt from pre-registration data was made before the 1st December registration deadline (see Table 8). In the meantime, the registration data have confirmed that the estimated volumes were not reliable. The high figures can however be an indication of relatively high historical use of the substance before REACH, without having any details on the time period.

Table 8: Information on 2-ethoxyethyl acetate tonnages according to pre-registration data

No. of companies	180
No. of companies pre-registrations	188
min t/a acc. No. of pre-registrations*	10034 t/a
max t/a acc. No. of pre-registrations*	28340 t/a

⁸ Council Regulation (EEC) No 793/93 of 23 March 1993 on the evaluation and control of the risks of existing substances

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

Information available after the registration deadline of 1st December 2010

No registration dossier for 2-EEA was submitted by the registration deadline of 1st December 2010. Given its classification as a CMR, this means that no company produces or imports 2-EEA in volumes higher than 1 t/year. Recently however, relevant number Classification and Labelling notifications have been submitted to ECHA. This provides a strong indication that the substance is still used in the EU, but at low tonnages.

1.1.1 Information from Product Register Data (SPIN database)

The SPIN database⁹ (Substances in Preparations in the Nordic Countries) was searched for information on 2-ethoxyethyl acetate in products on the national markets of Norway, Sweden, Finland and Denmark (2005-2008).

It is important to always remember that the use accounted for in SPIN is the use of substances in chemical products and preparations. Non-chemical products are not included. Thus the substance can very well be used and present in other kinds of products because the quantities refer to use in chemical products only.

As a result of secrecy considerations some substances in the Nordic product registers are only mentioned in SPIN by their name. Total quantities and the total number of products have not been reported to SPIN if the substance is contained in less than 4 products and is registered by less than 3 companies.

⁹ <http://195.215.251.229/DotNetNuke/default.aspx>

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 7 and 8 might be considered as overestimations.

Table 9: 2-ethoxyethyl acetate in products according to SPIN for 2005 – 2006.

Country	2005		2006	
	number of preparations	tonnage	number of preparations	tonnage
Norway	5	14.4	confidential	
Sweden	18	4	16	1
Finland	7	1	6	0.0*
Denmark	29	7.6	27	8.9
Total:		27.0 tons		9.9 tons

* “0.0 tons” means that the notified volumes were smaller than 0.1 tons.

Table 10: 2-ethoxyethyl acetate in products according to SPIN for 2007– 2008.

Country	2007		2008	
	number of preparations	tonnage	number of preparations	tonnage
Norway	7	1.5	confidential	
Sweden	15	1	15	0.0*
Finland	5	0.0*	8	8.9
Denmark	25	21.3	26	3.3
Total:		23.8 tons		12.2 tons

*“0.0 tons” means that the notified volumes were smaller than 0.1 tons.

1.1.2 Information from other Member States

France

In a report by AFSSET (2008) it is described that the use of 2-EEA in France has considerably decreased during the last decades (period '2000-2006' compared with period '1987-1998'), but some persistent uses are still remaining (21 preparations declared in SEPIA¹⁰ between 2000 and 2006). According to this report, 2-EEA is no more produced in Europe.

1.1.3 Conclusions on volumes

2-EEA is still present on the EU market. No registration dossier was introduced for this substance by the 1st December 2010 deadline. Several C&L notifications have however been made. Volumes of 2-EEA in the Nordic countries can be estimated from the Product Register Data (SPIN database);

¹⁰ 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.

in 2008, more than 10 tons of 2-EEA were registered for their use in chemical products and preparations.

1.2 Information on uses

1.2.1 EU RAR, 2008

According to the EU RAR, 2008, 2-EEA was mainly used as solvent in the chemical industry and for the formulation of paints, lacquers and varnishes for industrial use. 2-EEA was also used as an intermediate in the chemical industry. This information was based on historical information and considered to be no more relevant.

1.2.2 France

In a report by AFSSET (2008) the worker exposures are described as less frequent. It is still reported in the sector of rubber and plastic industry, in pneumatic spraying and serigraphy printing. Furthermore, one professional exposure of 2-EEA has also been measured in the chemical industry sector (monitoring data collected between 2000 and 2006). The report further refers to different investigations carried out on glycol ethers. 2-EEA has not been found in an investigation on use in garages, cleaning, hairdressing and general mechanics, carried out in 123 small and medium-sized enterprises (Beaujean et al., 2005), in a study on solvents carried out in 2004 by the INRS¹¹ (Triolet, 2005) nor in 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 (Communication DGCCRF 2007 from AFSSET). Concerning mixtures, glycol ethers classified as toxic to reproduction are practically not found in marketed mixtures (see Table 11). 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 1PG2ME or 1PG2MEA 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, 21 formulations which contain 2-ethoxyethyl acetate.

¹¹ INRS: Institut National de Recherche et de Sécurité

Table 11. Occurrence* of glycol ethers classified as toxic for reproduction (cat. 2) in formulations registered in SEPIA between 2000 and 2006.

Product category	total registered formulations	total number of formulations containing glycol ethers	total number of formulations 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

* a formulation can be counted several times if several uses are reported or if it contains several glycol ethers classified as reprotox cat.2.

1.2.3 Uses according to the SPIN database

The SPIN database was searched for industrial uses of 2-ethoxyethyl acetate. Data could be obtained from Denmark, Finland, Norway and Sweden. The industrial uses are presented in Table 12.

Table 12: Industrial Uses (NACE¹²) according to the SPIN database (2005-2008).

Country	Year	Code	Industrial Use	# Prep***	Tons**
DK	2005	35	Manufacture of other transport equipment n.e.c.	18	4.7
FIN	2005	24	Manufacture of chemicals and chemical products	4	1.0
FIN	2005	36	Manufacture of furniture; manufacturing n.e.c.		
FIN	2005	45	Construction		
S	2005	25	Manufacture of rubber and plastic products	3	0.0*
DK	2006	35	Manufacture of other transport equipment n.e.c.	17	3.4
FIN	2006	24	Manufacture of chemicals and chemical products		
FIN	2006	36	Manufacture of furniture; manufacturing n.e.c.		

¹² NACE (Nomenclature générale des activités économiques dans les Communautés européennes)

ANNEX XV – IDENTIFICATION OF SVHC – 2-ETHOXYETHYL ACETATE

FIN	2006	45	Construction		
DK	2007	35	Manufacture of other transport equipment n.e.c.	17	9.6
FIN	2007	24	Manufacture of chemicals and chemical products		
FIN	2007	45	Construction		
N	2007	35	Manufacture of other transport equipment n.e.c.	4	0.6
DK	2008	C25	Manufacture of fabricated metal products, except machinery and equipment	4	1.1
DK	2008	C30	Manufacture of other transport equipment	17	1.1
FIN	2008	C20	Manufacture of chemicals and chemical products	6	1.9
FIN	2008	C30	Manufacture of other transport equipment		

* 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 (2005-2007, DK, 9.6 tons/year) is given as “Manufacture of other transport equipment n.e.c.”. 2008 Finland registered 1.9 tons/year for industrial use category “Manufacture of chemicals and chemical products”.

In Table 13 national industry groups (based on NACE) from Denmark and Sweden are presented. They usually operate on a more detailed level than the 2 digit NACE code in Table 12. Therefore data that might be included in the overall presentation in the "Industrial use (NACE)" tab might be partly or totally suppressed in the "Industrial Use" tab due to confidentiality.

Table 13: Industrial Uses in DK and S (using national codes) according to the SPIN database (2005-2008)

Country	Year	Code	Use Category	# Prep	Tons*
S	2005	D25.2	Industry for plastic products	3	0.0
DK	2005	DM353000	Manufacture of aircraft and spacecraft	5	0.1
DK	2005	DM351000	Building and repairing of ships and boats	11	4.0
DK	2006	DM353000	Manufacture of aircraft and spacecraft	5	0.0
DK	2007	DM353000	Manufacture of aircraft and spacecraft	5	0.0
DK	2008	C303000	Manufacture of aircraft and spacecraft and related machinery	5	0.0

*The information “0.0 tons” means that the volume is below the limit of accuracy, which is 100 kg.

Additionally, the SPIN database was searched for use categories of 2-ethoxyethyl acetate in the Nordic countries (2005-2008). The use categories are presented in Table 14.

Table 14: Use categories (UC62) according to the SPIN database

Country	Year	Code	Use Category	# Prep**	Tons
FIN	2005	59	Paints, laquers and varnishes		
FIN	2005	48	Solvents		
FIN	2005	02	Adhesives, binding agents		
S	2005	48	Solvents	3	0.0*
DK	2005	48	Solvents	4	0.6
DK	2005	59	Paints, laquers and varnishes	13	0.8
FIN	2006	59	Paints, laquers and varnishes		
FIN	2006	48	Solvents		
FIN	2006	02	Adhesives, binding agents		
DK	2006	48	Solvents	4	0.3
DK	2006	59	Paints, laquers and varnishes	13	5.9
FIN	2007	48	Solvents		
FIN	2007	02	Adhesives, binding agents		
DK	2007	48	Solvents	4	0.7
DK	2007	59	Paints, laquers and varnishes	11	5.9
FIN	2008	59	Paints, laquers and varnishes		
FIN	2008	48	Solvents	6	1.9
DK	2008	48	Solvents	4	0.0*
DK	2008	59	Paints, laquers and varnishes	11	0.7

* 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.

The sum of "Industrial use" volumes and the "Total use" volume for a specific substance used in a specific country cannot be compared. Partly because a certain volume can be presented with more than one code, partly because the distribution on codes often results in a number of preparations below the limit of confidentiality, which means that code and volume cannot be presented.

In 2008, the following use categories (UC62) for 2-ethoxyethyl acetate have been notified in the SPIN database: Paints, laquers and varnishes, solvents.

1.2.4 Use restrictions

2-EEA is covered by entry 30 of Annex XVII of the REACH regulation: "substances which appear in Part 3 of Annex VI to Regulation (EC) No 1272/2008 classified as toxic to reproduction category 1A or 1B (Table 3.1) or toxic to reproduction category 1 or 2 (Table 3.2)". It shall therefore 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 legibly and indelibly as follows: "Restricted to professional users".

According to the Cosmetics Directive 76/768/EEC¹³, Annex II, No. 673, 2-ethoxyethyl acetate must not form part of the composition of cosmetic products.

Due to its boiling point of 156 °C at 1013hPa, 2-ethoxyethyl acetate falls under the definition as volatile organic compounds according to Directive 2004/42/EC¹⁴ on the limitation of emissions of volatile organic compounds regarding the use of organic solvents in certain paints and varnishes and vehicle refinishing products.

An occupational exposure limit value for 2-ethoxyethyl acetate according to Directive 98/24/EEC¹⁵ has been established at community level with the implementation of Commission Directive 2009/161/EU¹⁶ of 17 December 2009 establishing a third list of indicative occupational exposure limit values. For 2-EEA an 8 hour time weighted average (TWA) of 11mg/m³ (or 2ppm) is given with a special remark noting the possibility of significant uptake through the skin (skin notation, see Table 16)).

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

14 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

15 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)

16 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

According to the EU RAR, a voluntary program of industry was implemented in 1998 in order to monitor the end use applications of glycol ether solvents, including 2-EEA. The distributors and customers of this chemical have to ensure that 2-EEA is not used in consumer goods, household products, cosmetics and other applications where exposure is poorly controlled. 2-EEA is also recommended not to be used in the European Printing Ink Industry, as it is included in the EuPIA Exclusion List of raw materials for the European Printing Ink Industry¹⁷.

1.2.5 Conclusions on uses

2-EEA was used in the past as solvent and intermediate in the chemical industry. It was also used for the formulation of paints, lacquers and varnishes for industrial use.

Based on available information, 2-EEA is still used on the EU market, as solvent and for the formulation of paints, lacquers and varnishes for professional use exclusively, but at very low volumes. These remaining uses are probably very specific, as suggested, for instance, by the following use category: Building and repairing of ships and boats, Manufacture of aircraft and spacecraft (see Table 13).

1.3 Information on exposure

1.3.1 Human Exposure

1.3.1.1 General Information

As a result of its adverse reproductive effects 2-ethoxyethyl acetate 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 may not contain 2-EEA any longer.

The last years have seen a decline in the use of 2-EEA. The substance is still used nowadays in European Industries, at low volumes.

The area of concern is occupational exposure to 2-EEA. Inhalation and dermal exposure is expected for workers.

1.3.1.2 Occupational Exposure

Within the EU different Occupational exposure limits (OEL) exist (Table 15).

¹⁷ http://www.eupia.org/EPUB/easnet.dll/GetDoc?APPL=1&DAT_IM=020A3B&TYPE=PDF

Table 15: Occupational exposure limit values (OEL) applied in different EU countries¹⁸

Country	8-hour limit value (mg/m ³)	Short term limit value (mg/m ³)
Austria	27mg/m ³	108 mg/m ³
Belgium	27 mg/m ³	
Czech Republic	25 mg/m ³	50 mg/m ³
Finland	11 mg/m ³	
France	27 mg/m ³	-
Poland	11 mg/m ³	
Portugal	27 mg/m ³	
Sweden	30 mg/m ³	50 mg/m ³

An indicative occupational exposure limit value for 2-ethoxyethyl acetate 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 16).

Table 16: 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	
111-15-9	2-ethoxyethyl acetate	11	2	-	-	skin

Sufficient data were not available to recommend a STEL. A "skin" notation is recommended as dermal absorption can contribute substantially to the total body burden.

A biological limit value (BLV), measured at the end of the work week, is set to 50 mg 2-ethoxyacetic acid/l urine (40 mg 2-ethoxyacetic acid/g creatinine) (SCOEL, 2007).

Workplace Exposure Data

France:

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

The data in table 17 show that exposure concentrations of 2-EEA declined from the period 1987-1998 to the period 2000 – 2006.

¹⁸ <http://osha.europa.eu/en/publications/reports/548OELs>; <http://www.arbeitsinspektion.gv.at/NR/rdonlyres/F173280B-D4FB-44D2-8269-8DB2CB1D2078/0/GKV2007.pdf> (for the Austrian OEL); <http://www.abc.com.pl/serwis/du/2009/0873.htm> (for the Polish OEL).

Table 17: Exposure Measurements conducted between 1987-1998 and between 2000-2006

Period	No. of measurements with professional exposure to 2-EEA	Exposure concentration (mg/m ³) of 2-EEA			
		mean	median	95-percentil	maximum
1987-1998	913	8.6	3	39	183
2000-2006	24	5.42	3.63	19.30	23.80

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

In tables 18 and 19, a detail of the measurements between 2000 and 2006 is given per sector of activity and per workstation.

Table 18: Exposure Measurements per sector of activity (between 2000 and 2006)

Sector of activity	No. of measurements	Exposure concentration (mg/m ³) of 2-EEA			
		mean	Range of measurements	Median	95-percentil
Chemical industry	1	7.0	-	-	-
Rubber and plastic	16	6.2	0.05-23.8	3.3	23.8

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

Table 19: Exposure Measurements per workstation (between 2000–2006)

Workstation	No. of measurements	Exposure concentration (mg/m ³) of 2-EEA	
		mean	Range of measurements
pneumatic spraying	8	0.2	0.05-0.1
serigraphy printing (drivers of manual or automatic machines for serigraphy)	8	12.2	6.0-23.8

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

2. CURRENT KNOWLEDGE ON ALTERNATIVES

According to TRGS 609 (TRGS 609, 1992) the use of alternative substances as a solvent in lacquer and plastic industry must 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, 1-methoxy-2-propyl acetate, 2-butoxyethanol, 2-butoxyethyl acetate, ethyl-3-ethoxypropionate were mentioned as possible substitutes for methoxyethanol, ethoxyethanol and their acetates. According to TRGS 609/1992 these substances can be used as alternatives regarding their toxicological properties, which were presented. Information on alternative substances for other uses was not available in this paper.

According to OSHA (OSHA 2003) use of 2-methoxyethanol, 2-ethoxyethanol and their acetates has largely been replaced by less-toxic substitutes; ethylene glycol butyl ethers from the E-series, P-series glycol ethers (propylene glycol ethers), and ethyl-3-ethoxypropionate. Ethylene glycol

monobutyl ether acetate, diethylene glycol monobutyl ether acetate and propylene glycol monomethyl acetate have replaced the use of 2-EEA.

3. RISK-RELATED INFORMATION

3.1 Human Health Risk Assessment

According to the guidance on information requirements and chemical safety assessment (Chapter R.8: Characterisation of dose [concentration]-response for human health, Appendix R 8-13), when an European Union IOELV exists, it can be used in place of developing a DNEL. This approach has been followed here.

Health effects

The main considerations of the Recommendation from the SCOEL¹⁹, 2007 were compiled in this section.

Proposal by Sweeney et al., 2001

Physiologically based pharmacokinetic models of Gargas and coworkers (Gargas et al., 2000) for 2-ethoxyethanol and 2-ethoxyethyl acetate in pregnant rats and humans were used with data from developmental toxicity studies with pregnant rats (Doe, 1984) and from 4 volunteer studies (non-pregnant) with 4 hour exposure to 2-ethoxyethyl acetate conducted by Groeseneken and coworkers (Groeseneken et al., 1986 a, b and 1987 a, b). The models considered 5 compartments, rapid hydrolysis from 2-ethoxyethyl acetate to 2-ethoxyethanol, metabolism from 2-ethoxyethanol to 2-ethoxyacetic acid and its elimination in urine. Physiological parameters for an average pregnant woman were used to calculate human-equivalent NAEL (no adverse effect level) estimates, based on internal concentrations in rats exposed at previously determined NOAEL for developmental toxicity (50 ppm)²⁰. The NAEL was estimated to be 25 ppm. An 8-h OEL of 2 ppm is therefore proposed, by dividing the human-equivalent NAEL of 25 ppm by default uncertainty factors (2.5 for interspecies, 3.16 for interindividual variability and 1.8 for intraspecies pharmacokinetic differences) (Sweeney et al., 2001).

Biological monitoring

In the SCOEL/SUM/116 paper, biological monitoring studies were reported. In some of them higher metabolite concentrations were found in the urine than the values expected from the data from Groeseneken et al. (1986 a, b and 1987 a, b) for the air concentrations measured for 2-ethoxyethanol and 2-ethoxyethyl acetate. It was concluded that the substances are readily absorbed by the intact skin and this is the main route of absorption at most workplaces.

Recommendation of the SCOEL

¹⁹ 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>)

²⁰ In Doe (1984) 25 ppm was the NOAEL for 2-EEA. However, a NOAEL of 50 ppm (as determined for EGEE) might also be valid for 2-EEA, as supported by the findings of Tyl et al. (1988).

The critical effects of 2-ethoxyethyl acetate are on reproduction and the blood, which are detected in experimental animals and in humans. As humans are more sensitive than animals, only human studies (even if they are of limited validity) were used for deriving the OEL. If dermal absorption is avoided, an 8-h TWA²¹ of 2 ppm should protect from effects on haematopoiesis 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. This 8-h TWA of 2 ppm is in accordance with the OEL value of 2 ppm proposed by Sweeney et al. (2001).

Exposure and risks

Available exposure data are quite limited. Professional exposure measurements of 2-EEA in France during the period 2000-2006 (see section 1.3.1) show values higher than the IOELV, e.g. for serigraphy printing. Based on these data, a risk for workers cannot be excluded.

²¹ Time-weighted Average (TWA): In air sampling, the average air concentration of contaminants during a given period.

REFERENCES

AFSSET, Agence française de sécurité sanitaire de l'environnement et du travail (2008): Les éthers de glycol. Synthèse des connaissances sur les expositions de la population générale et professionnelle en France, Septembre 2008. http://www.afsset.fr/upload/bibliotheque/275806516259413151865520013551/ethers_glycol_sept08.pdf

Beaujean M., Biolchini R., Bouniol L., et al. (2005): Utilisation d'éthers de glycol: une enquête dans les PME. Document pour le médecin du travail n°101. Institut National de Recherche et de Sécurité (INRS). 1^{er} trimestre 2005. 101 TF 139. Pp 65-74.104 TF 144.

Chemsafe (1996) : National database for safety data of the Physikalisch-technische Bundesanstalt Braunschweig, established by expert judgement.

DGCCRF (2007)

Direction générale de la concurrence, de la consommation et de la répression des fraudes (DGCCRF). (2007). http://www.minefi.gouv.fr/directions_services/dgccrf/ Consulted in Septembre 2007.

Doe JE, 1984. Ethylene glycol monoethyl ether and ethylene glycol monoethyl ether acetate teratology studies. Environm. Health Perspect. 57, 33-41.

ECETOC, August 1995. Technical Report No. 64, The toxicology of glycol ethers and its relevance to man.

EU RAR final, 2008 : European Union Risk assessment report, 2-ethoxyethyl acetate: http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/2ethoxyethylacetatereport067.pdf

Gargas ML, Tyler TR, Sweeney LM, Corley RA, Weitz KK, Mast TJ, Paustenbach DJ, Hays SM (2000) A toxicokinetic study of inhaled ethylene glycol ethyl ether acetate and validation of a physiologically based pharmacokinetic model for rat and human. Toxicol Appl Pharmacol 165: 63-73.

Groeseneken D, Veulemans H, Masschelein R (1986 a) Respiratory uptake and elimination of ethylene glycol monoethyl ether after experimental human exposure. Br J Ind Med 43: 544-549.

Groeseneken D, Veulemans H, Masschelein R (1986 b) Urinary excretion of ethoxyacetic acid after experimental human exposure to ethylene glycol monoethyl ether. Br J Ind Med 43: 615-619.

Groeseneken D, Veulemans H, Masschelein R, van Vlem E (1987 a) Pulmonary absorption and elimination of ethylene glycol monoethyl ether acetate in man. Br J Ind Med 44: 309-316.

Groeseneken D, Veulemans H, Masschelein R, van Vlem E (1987 b) Ethoxyacetic acid: a metabolite of ethylene glycol monoethyl ether acetate in man. Br J Ind Med 44: 488-493.

Hardin BD, Goad PT and Burg JR, 1984. Developmental toxicity of four glycol ethers applied cutaneously to rats. Environ. Hlth. Persp. 57, 69-74.

Hüls AG (1989) : Verteilungskoeffizient n-Octanol – Wasser für „Altstoffe“; Test report from 10.01.1989.

Johansen Dynesius: Liquid-air partition coefficients of six commonly used glycol ethers. Br J Ind Med 45(8):561-564.

Kirk-Othmer (1980): Encyclopedia of chemical technology, 3rd ed., vol 11; John Wiley & Sons, Inc. 1980.

Merck-Index (1989):

Susan Budavari, ed. 1989. The Merck index. 11th edition. Rahway, NJ: Merck & Co., Inc.

Nagano K, Nakayama E, Koyano M, Oobayashi H, Adachi H and Yamada T, 1979. Testicular atrophy of mice induced by ethylene glycol mono alkyl ethers. Jap. J. Ind. Health 21, 29-35.

Nelson BK, Setzer JV, Brightwell WS, Mathinos PR, Kuczuk MH, Weaver TE and Goad PT, 1984. Comparative inhalation teratogenicity of four glycol ether solvents and an amino derivative in rats. Environ. Health Persp. 57, 261-271.

OSHA (2003). Occupational Safety and Health Administration. Occupational Exposure to 2-methoxyethanol, 2-Ethoxyethanol and their Acetates (Glycol Ethers). Withdrawal of proposed rule. Federal Register Vol 68, No. 250 p.75475-75476.

(http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=FEDERAL_REGISTER&p_id=18049)

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>

Sweeney LM, Tyler TR, Kirman CR, Corley RA, Reitz RH, Paustenbach DJ, Holson JF, Whorton MD, Thompson KM, Gargas ML (2001) Proposed occupational exposure limits for select ethylene glycol ethers using PBPK models and Monte Carlo simulations. Toxicol Sci 62: 124–139.

TRGS 609 (1992): Technical Rules for Hazardous Substances. In German: Technische Regeln für Gefahrstoffe, Ersatzstoffe, Ersatzverfahren und Verwendungsbeschränkungen für Methyl- und Ethylglykol sowie deren Acetate; Federal Institute for Occupational Safety and Health. http://www.baua.de/cln_104/de/Themen-von-A-Z/Gefahrstoffe/TRGS/TRGS-609.html

Triolet J. (2005): Panorama de l'utilisation des solvants en France fin 2004. Note documentaire 2230-199-05. Hygiène et Sécurité du Travail. Cahier de notes documentaires. Institut National de Recherche et de Sécurité (INRS). 2^{ème} trimestre 2005-199.

Tyl RW, Prittis IM, France KA, Fisher LC, Tyler TR (1988) Developmental toxicity evaluation of inhaled 2-ethoxyethanol acetate in Fischer 344 rats and New Zealand white rabbits. Fundam Appl Toxicol 10: 20-39.

ANNEX

Summary of reproductive toxicity

2-ethoxyethyl acetate has been classified as toxic for the reproduction on the basis of the following elements (Table 20 gives an overview of the, at that time, key studies. No further literature study was carried out):

Fertility

Reduced testis weight, which was dose –dependent, and testicular atrophy were noted at 1000 mg/kg/day or more, administered orally in mice (Nagano *et al.*, 1979).

Effects on foetus

Inhalation exposure of rats to 130 ppm or more during pregnancy resulted in teratogenicity and foetotoxicity in the absence of any signs of maternal toxicity. Complete litter resorption occurred at 600 ppm (Nelson *et al.*, 1984).

In rabbits, maternal toxicity, teratogenicity and foetotoxicity were seen at 400 ppm. At 100 ppm there were signs of foetotoxicity in the absence of maternal toxicity and 25 ppm was a no-effect level (Doe, 1984).

Dermal application of approximately 6000 mg/kg/day to pregnant rats resulted in significant foetotoxicity, teratogenicity with only slight maternal toxicity (Hardin *et al.*, 1984).

Table 20: key studies* considered for the classification of 2-EEA as toxic for reproduction

	Species (Strain)	Route	Animals per dose level	Time	Exposure conc. or dose	Response	Reference
Repeated dose toxicity study	Mice (ICL-ICR)	oral	5 m/5 f	5 wk	0 mg/kg	-	Nagano <i>et al.</i> , 1979
					500 mg/kg	No effects.	
					1000 mg/kg	Testicular atrophy.	
					2000 mg/kg	Testicular atrophy.	
					4000 mg/kg	Testicular atrophy.	
Reproduction and Developmental studies	Rats (Sprague-Dawley)	Inhalation (whole body)	9-20 f	g.d. 7-15 (7h/d)	0 ppm	-	Nelson <i>et al.</i> , 1984
					130 ppm	↓foetal weight, skeletal variations.	
					390 ppm	↓foetal weight, ↑resorptions/litter; skeletal and visceral malformations.	
					600 ppm	100% resorption.	
	Rabbits (Dutch)	Inhalation	24 f	g.d. 6-18 (6h/d)	0 ppm	-	Doe, 1984
					25 ppm	No effects.	
					100 ppm	↓foetal weight, ↑postimplantation loss, skeletal and visceral variations.	
	Rats	dermal	18 f	g.d. 7-16	0 mg/kg	-	Hardin <i>et al.</i> , 1984
					5923 mg/kg	↑postimplantation loss. ↑cardiovascular and skeletal malformations.	

Conversion factor for 2-EEA (20°C, 101 kPa): 1 ppm = 5.494 mg/m³; 1 mg/m³ = 0.182 ppm

*compiled from Document XI/002/92 of the 13th meeting of specialized experts on 31st of March and 1st of April 1992 and from the ECETOC Technical Report No.64, 1995 (with additional information from the 3 papers : Nelson *et al.*, 1984; Doe, 1984 and Hardin *et al.*, 1984).