THIS DOCUMENT HAS BEEN PREPARED ACCORDING TO THE PROVISIONS OF ARTICLE 136(3) “TRANSITIONAL MEASURES REGARDING EXISTING SUBSTANCES” OF REACH (REGULATION (EC) 1907/2006). IT IS NOT A PROPOSAL FOR A RESTRICTION ALTHOUGH THE FORMAT IS THE SAME

ANNEX XV TRANSITIONNAL REPORT

SUBMITTED BY: France

DATE: 20.11.08

SUBSTANCE NAME: **PGME** (monomethyl ether of propylene glycol)
IUPAC NAME: **1-METHOXYPROPAN-2-OL**
EC NUMBER: 203-539-1
CAS NUMBER: 107-98-2

A. SUMMARY

PGME has a very low acute toxicity by all routes of exposure. Repeated dose toxicity show few hepatic effects after inhalation exposure and by oral route CNS reversible effects were seen at all tested doses leading to a R67 classification proposal. Based on the toxicological profile and risk assessment analysis and considering that the risk management measures in already in place and enforced, we consider that restriction is not appropriate.

B. INFORMATION ON HAZARD AND RISK

Unless specified in the text as another reference, and instead the paragraph B.9, this part has been agreed by TCNES based on the RARs [1;2]. Only summaries are reported here, more details are available in the documents attached in the technical dossier and cited in reference.

B.1 Identity of the substance(s) and physical and chemical properties

This part has been agreed by TCNES based on the RAR finalised the 28th October 2008 [1].

B.1.1 Name and other identifiers of the substance(s)

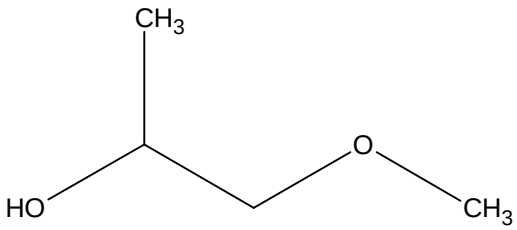
CAS Number: 107-98-2

EINECS Number: 203-539-1

IUPAC Name: 1-methoxypropan-2-ol

Molecular formula: $C_4H_{10}O_2$

Structural formula:



Molecular weight: 90.1 g/mol

Synonyms: 1-methoxy-2-hydroxypropane; 1-methoxy-2-propanol; 1-methoxypropanol-2; 1-methoxypropane-2-ol; 2-methoxy-1-methylethanol; 2-propanol-1-methoxy; methoxy Propanol; methoxypropanol; monomethyl ether of propylene glycol; monopropylene glycol methyl ether; PGME; propylene glycol methyl ether; propylene glycol monomethyl ether; éther 1-méthylique d'alpha-propylèneglycol; éther monométhylique du propylène-glycol

In this assessment, the name PGME will be used for the substance, as this is the more common name.

B.1.2 Composition of the substance(s)

The commercially supplied product is usually a mixture of two isomers 1-methoxypropan-2-ol (PGME, alpha isomer) and 2-methoxypropan-1-ol (beta isomer, CAS n°1589-47-5).

PGME is the main compound, totalizing 99.5 % of the product with less than 0.5 % of 2-methoxypropan-1-ol, considered as an impurity.

No additive is contained in the marketed product.

B.1.3 Physico-chemical properties

Table 1.1: Summary of physico-chemical properties of PGME

Property	Value
Physical state	Liquid
Melting point	-96°C
Boiling point	120°C
Relative density	0.921 g/cm^3
Vapour pressure	16.4 hPa at 25°C
Water solubility	Fully miscible, 500 g/l
Partition coefficient n-octanol/water (log value)	-0.49
Flash point	32°C
Autoflammability	278°C
Henry's constant	0.12 Pa.m^3/mol

B.1.4 Justification for grouping

No grouping proposed.

B.2 Manufacture and uses

This part has been agreed by TCNES based on the RAR [2].

B.2.1 Manufacture and import of a substance

B.2.1.1 Production processes

In the production process methanol and propylene oxide are reacted at a pressure of 26 bar and a temperature ranging from 95 to 180°C. The reaction is catalysed homogeneously in closed system. The reaction product is separated in a number of distillation steps. Excess methanol is recovered in the first distillation column and recycled back to the reactor. The

desired PGME product, 1-methoxy-2-propanol, is recovered in the second distillation column. The by-product 2-methoxy-1-propanol is recovered in the third column and stored for subsequent conversion. The bottom stream is recycled and reused as catalyst (Personal communication Shell, 20/01/03).
Main producers have continuous production plants (24 hours per day, 7 days a week) with continuous feed and outlet (Personal communication Dow, 19/02/02).

B.2.1.2 Production capacity

The production and sales data for years 2001 to 2003 are given by the **Table 2.1**

Table 2.1 Overview of PGME production and sales in Europe for years 2001 to 2003 (data provided by CEFIC, 2004)

In tonnes	2001	2002	2003	Figures retained
Production	171,000	185,400	188,000	188,000
Imports	0	0	0	0
Exports	29,500	42,500	50,000	46,000
Net into stock	2,000	-1,500	-500	-
Captive use (PGMA production)	53,500	61,000	56,500	58,500
Sales in EU	86,000	83,400	82,000	83,500
Total use in EU	**139,500**	**144,400**	**138,500**	**142,000**

The figures presented above show that there is a trend for an increase in production year by year: 171, 185.4 and 188 kt for years 2001, 2002 and 2003, respectively. However this is almost entirely due to increased demand for exports: 29.5, 42.5 and 50 kt each year between 2001 and 2003. The overall demand within the EU remains flat. PGME is currently manufactured with volumes exceeding 1,000 tonnes/year by five producers in the EU (see **Table 2.2**).

PGME is currently manufactured with volumes exceeding 1,000 tonnes/year by five producers in the EU (see **Table 2.2**).

Table 2.2: Main producers of PGME

Company	Localisation
BASF	Ludwigshafen (Germany)
Lyondell*	Rotterdam (Netherlands)
BP	Lavera (France)
Dow	Stade (Germany)
Shell	Hoogvliet (Netherlands)

* LYONDELL acquired ARCO in 1998

According to personal communication from BP (20/05/03), BP stopped its production of PGME.

In a more recent French study, it is indicated that, according to data updated in 2005 and supplied by OSPA, 280,000 tonnes a year of PGME are produced in Europe (against 170,000 tonnes in 2000). The amount sold in Europe each year is 117,000 tonnes.

B.2.2 Uses

The industrial and use categories of PGME are summarised in Table 2.3. PGME is mainly used as solvents. The dimmed lines correspond to negligible uses. A breakdown of the uses of PGME in Europe has been established based on the data collected for years 2001 to 2003 by CEFIC (2004) (see Table 2.3). The total used tonnage recorded is 142,000 tonnes taking into account the captive use. The analysis of this set of data has led to a choice which is meant to represent a reasonable worst case. The final data choice is based mainly on averages but some expert judgement has also been applied to adjust for market knowledge and the fact that supply via distributors adds some uncertainty to the numbers. Typically, 25-40% of volume goes via distributors. To reflect these uncertainties, the figures are quoted as rounded numbers. 2002 and 2003 data should be given more weight as some errors have possibly been made during assessment of the 2001 data in allocating users to the appropriate end use categories.

Table 2.3 continued Use of PGME in the EU

End use	**Stage of the life cycle**	**Industry category**	**Use category**	**2001**	**2002**	**2003**	Retained proposal	
							Quantity used (tonnes)	**Percentage** of total **use**
Printing inks*	Formulation Processing	12: pulp, paper and board industry	48: Solvent	11,793	12,000	12,000	12,000	8.5%
Others*	Formulation Processing	16: other	55: other	11,586	0	0	0	0
Detergents, cleaners	Formulation Private/public use	5: Personal/ domestic 6: Public domain	48: Solvent	4,345	7,000	7,700	7,500	5.3%
Leather finishing agent	Processing	7: Leather processing industry	48: Solvent	517	2,900	400	1,900	1.3%
Electronic industry	Processing	4: Electrical/ electronic industry	48: Solvent	2,069	1,300	1,500	1,500	1%
Agriculture	Processing	1: agricultural industry	48: Solvent	0	1,100	1,200	1,150	0.8%
Cosmetics/ Personal care	Formulation Private use	5: Personal/ domestic	48: Solvent	1,655	700	700	1,000	0.7%
Adhesive		5: Personal/ domestic	48: Solvent	207	400	500	400	0.2%
Metal cleaning		6: Public domain	48: Solvent	0	400	400	400	0.2%
Oil spill dispersant/ Oilfield chemicals		6: Public domain	48: Solvent	103	100	200	150	0.1%
Total				**139,500**	**144,400**	**138,500**	**142,000**	**100%**

* For these end uses there is a possibility that formulation and processing steps take place at a same site. These cases will be treated during risk characterisation.

According to the other glycol ethers, 10% of paints and coating are used at private level and 90% are used at industrial level

Over the past two decades, ethylene glycol methyl ether and ethylene glycol ethyl ether have progressively been replaced by propylene glycol derivatives. The main uses of PGME are in paints or surface coatings (solvent-based or water-based), followed by cleaners and printing inks. Other minor uses reported are solvent in the electronic industry, in cosmetics/personal care (capillary tinting, nail-varnish removers), leather finishing agents, adhesives, agricultural and oil field chemicals.

According to the SIDS initial assessment profile (2001), PGME is used in the manufacture of PGME acetate as well as in a wide variety of industrial and commercial products, including paints and varnishes (30% for surface coatings), printing inks (6%), cleaners (23%), adhesives and electronics (7%).

In the Swedish product register (KEMI 2002), 906 products containing PGME (of which 250 were private household products) have been identified: 59 % are paints (or hardeners for paints), varnishes or adhesives, 9 % cleaning agents, 5 % dyestuffs and 5 % diluents.

In the Danish product register (Danish EPA, 2004), 3387 products containing PGME have been identified,. The most common uses were paints, lacquers and varnishes (74 %), solvents (4 %), cleaning/washing agents (5 %) and process regulators (4 %).

Other data extracted from the French product register SEPIA (INRS 2003) showed that 243 products registered between 1997 and 2002 contained PGME. The main use category was: paints, varnishes and inks (45 %).

Dentan et al (2000) analysed the chemicals registration database in Switzerland in order to identify users of PGME and potential exposure. In 1999, out of 150,000 products, 2,334 were found to contain PGME and most between 1% and 10% PGME. There was a great increase in the number of products declared between 1983 and 1991, which reflects the trend to replace certain ethylene glycol ethers by propylene glycol ethers. The most common uses were inks, paints and varnishes (50 %), solvents, diluents and pickling solutions (13 %), cleaning agents (10 %), glues, mastics and jointings (5 %), auxiliary materials (5 %).

The distribution of concentration intervals in the main type of products is presented in the tables 2.4, 2.5 and 2.6.

Table 2.4: Concentration of PGME in the main use categories in the Danish product register (2001)

Content %	Cleaning agents	Solvents	Paints		Process regulators	
[0-2]	22	45	2071		44	
]2-20]	101	50	406		57	
]20-50]	28	28	31		22	
]50-100]	7	22	52		23	

Table 2.5: Concentration of PGME in the main use categories in the French product register SEPIA (INRS, 2003)

Concentration (%)	Paints, varnishes and inks	Metallurgical and mechanical sectors products	Cleaning products

[0-1]	15	1	-
]1-5]	34	3	10
]5-10]	17	1	1
]10-20]	25	2	4
]20-50]	7	2	2
]50-100]	5	1	2

Table 2.6: Concentration of PGME in the main use categories in the Swiss product register (2000)

Concentration (%)	Inks, varnishes and paints	Solvents, diluents, pickling solutions	Glue, mastics, jointing	Cleaning agents	Auxiliary materials
[0-1]	141	8	14	19	11
]1-10]	667	130	71	171	45
]10-30]	237	86	26	37	40
]30-50]	62	45	12	11	14
]50-100]	66	29	3	8	12

B.2.3 Uses advised against by the registrants

No data available.

B.2.4 Description of targeting

The major occupational routes of exposure to PGME are inhalation and skin contact. Assuming proper hygiene measures are applied, oral exposure would normally not occur in the workplace.
Workers may be significantly exposed during the production of PGME, its processing as an intermediate or during the formulation and use of PGME containing products. Occupational exposure assessment will be carried out through three main categories of scenarios:
(a) manufacture of PGME and its use as an intermediate;
(b) formulation of products containing PGME;
(c) use of products containing PGME.
The third category will focus on particular sub-scenarios for exposure in the most frequent type of use, or particular pattern of use, when relevant.

B.3 Classification and labelling

B.3.1 Classification in Annex I of Directive 67/548/EEC

PGME is listed in annex I according to the 19th ATP to Directive 67/548/EEC under index number: 603-064-00-3 as R10; S2-24. No classification for health effects.

B.3.2 Classification in classification and labelling inventory/Industry's self classification(s) and labelling

No data available.

B.4 Environmental fate properties

This part has been agreed by TCNES. Details can be found in the RAR [2].

B.4.1 Degradation

As no biodegradation rates are available for surface freshwater, surface saltwater, soil and sediment, the following rate can be estimated according to the procedure outlined in the TGD (EC, 2003):

Table 4.1 Estimation of biodegradation rate constants in the different compartments

Compartment	**Biodegradation rate (d 1)**
Surface freshwater	Kfreshwater = $4.7 . 10^{-2}$
Surface saltwater	Ksaltwater = $1.4 . 10^{-2}$
Sediment	Ksed = $2.3 . 10^{-3}$
Soil	Ksoil = $2.3 . 10^{-2}$

B.4.2 Environmental distribution

Based on an Air-biota-sediment-soil-water compartment model (EQC model v1.0 based on the level I fugacity model developed by Mackay), water is the preferential target compartment at equilibrium.

B.4.3 Bioaccumulation

No experimental data is available on bioaccumulation.
Using a QSAR (BCFWIN v2.14), a BCF of 3.16 was estimated. This value will be used for the risk assessment (US EPA and Syracuse Research Corporation, 2001).
In conclusion, PGME has a low potential for accumulation in biota.

B.4.4 Secondary poisoning

As PGME is not classified T+, T or Xn and as the potential for bioaccumulation is very low, secondary poisoning can be considered to be negligible.

B.5 Human health hazard assessment

This part has been agreed by TCNES based on the RAR finalised the 28th October 2008 [1]. For more details, please refer to this document.

B.5.1 Toxicokinetics

PGME is readily absorbed via oral and inhalation route. An absorption percentage of 100 % can be taken into account for these routes. Human data have shown that dermal absorption of vapour via the skin is limited. When exposed whole-body (normal clothing), PGME vapour provided contribution of approximately 4-8 % to the total body burden. An *in vitro* absorption rate of 1.17 mg/cm^2/h was estimated for pure PGME on human skin. If the dermal absorption of liquid PGME is compared to other glycol ether, the available data show that PGME is less absorbed than EGBE (it is estimated that PGME is twice less absorbed that EGBE). According to this data, it is proposed to take into account a dermal absorption factor of 30 % for liquid PGME (as EGBE – see EGBE RAR) considering that this is a worst case value.

According to the PbPk model, vapour PGME absorbed through the skin in humans contributed to about 5 to 10 % to the total body burden of PGME. If adjustments need to be made for the risk characterisation, the value of 10 % will be taken as a worst case value.

Also according to this model, maximum concentration of blood PGME are about 2.5 fold higher in rats than in humans after a 6h inhalation exposure at the same exposure level, for exposure levels above 100 ppm. For exposure concentrations below 100 ppm, the rat and human blood levels of PGME are similar which leads to the use of a factor of 1 instead of 0.4 in this range of concentrations.Main target organs were liver, thymus and spleen (concentration > blood levels after oral dosing). Little amount of PGME or metabolites were found in fat or testes. According to the data available, PGME does not seem to accumulate in the body.

The main metabolic pathway of PGME is O-demethylation leading to PG formation. This mechanism is easily saturable. Other paths are glucurono- and sulfo-conjugation. PG is excreted via urine or enters metabolic pathways to produce CO_2. At high dose, saturation of the metabolic pathways led to urinary elimination of PGME as such (see figure 4.23: metabolic pathway of PGME). PGME and metabolites are rapidly eliminated.

It appears that in rats, there is a sex difference in metabolism of PGME, females eliminating faster than males.

B.5.2 Acute toxicity

Information available suggests that the acute toxicity of PGME is very low.

The oral LD_{50} value for PGME in experiments in rats ranges from 4016 to 7,510 mg/kg. Oral LD_{50} values from other animal experiments were 10,800 mg/kg for mice; 1,840 to 5,300 mg/kg for rabbits, and 4,600 to 9,000 mg/kg for dogs.

Similarly, LC_{50} values were > 6,000 to 15000 ppm (22,440 to 54,600 mg/m^3) for rats; < 6,038 to 7,559 ppm for mice (22,600 to 28.300 mg/m^3), and > 14600 ppm (54,600 mg/m^3) for guinea pigs.

When applied occluded to the skin of rabbits, the LD50 value was found to be in the range of 13-14 g/kg. The acute (24 hr) percutaneous LD50 of the undiluted test material in rats was greater than 2000 mg/kg (the maximum dose that could be applied).

CNS depression has been observed in both humans and animals as a lead, single exposure effect. The lowest value for CNS depression in animals was seen in a RDT inhalation toxicity (3000 ppm, derived from the 2 year studies) leading to a NOAEC of 1000 ppm. In humans, a NOAEL of 750 ppm was derived for CNS depression, this value will be taken into account for the risk characterisation of acute effects. A classification R67 is needed for this end-point.
By dermal route, no systemic effects were seen at doses of 1000 mg/kg in a 21 day study. Only local effects limited to slight inflammation were seen.

No other classification is needed for PGME for acute toxicity whichever the route of exposure.

Table 5.1: Summary of acute toxicity					
	Species	LD50 / LC50	Experimental conditions / Effects	Validity	Reference
Inhalation	F344 rat	> 7559 ppm (28.3 mg/l)	Lethargy, decrease in body weight. No death	+	Ciezlak, 1991
	Rat	10000-15000 ppm (37.4 – 56.1 mg/l)	7hr treatment period: 5000 ppm no death 6hr treatment period: 10000 ppm LC50 4hr treatment period: 15000 ppm LC50	+/-	Rowe, 1954
	Rat		6hr treatment period LC_0 10000 ppm(36.4 mg/l) 4hr treatment period LC_0 1000 ppm (3.7 mg/l)	+/-	Smyth, 1962
	Rat	> 1600 ppm (6 mg/l) > 6400 ppm (24 mg/l)	4hr treatment period concentration 25.5, 36.4 and 54.6 mg/l for periods varying between 1 and 8 hrs	+	Gelbke, 1983
	Mouse B6C3F1	< 6083 ppm (22.6 mg/l)	6hr treatment period, 2 concentration tested (6038 and 7559 ppm). For the 6038 doses 4/5 death. CNS effects and reversible decrease of mean body weight	+	Ciezlak, 1991
	Rabbit	LD50 14600 ppm (54.6 mg/l)	7hr treatment period	+/-	Rowe, 1954

	Guinea pig	LCLo 14600 ppm (54.6 mg/l)	10 hr treatment period 7hr treatment period with 18.75 mg/l: no effects	+/-	Rowe, 1954
Dermal	Rabbit	13000 mg/kg	6 doses: 5000 to 14000 mg/kg. 24 hr exposure period, occlusive. CNS symptoms and slight skin irritation.	+/-	Rowe, 1954
	Rabbit	14100 mg/kg	Only LD50 reported	+/-	Smyth, 1962
	Rabbit	> 2000 mg/kg	24 hr treatment period.	+	Shell, 1985
Oral	Rat	6100 mg/kg	9 doses groups	+/-	Rowe, 1954
	Rat	7510 mg/kg	LD50: β isomer 5710 mg/kg	+/-	Smyth, 1941
	Rat	5200 mg/kg	Only LD50 reported	+/-	Smyth, 1962
	Rat	> 5000 mg/kg	Only LD50 reported	+	BASF, 1979
	Rat	5900 mg/kg	Only LD50 reported	+/-	BASF, 1964
	Rat	4016 mg/kg	CSN effects	+	Shell, 1985
	Mouse	10800 mg/kg	Only LD50 reported	+/-	Stenger, 1972
	Rabbit	> 1840 mg/kg	Only LD50 reported	+/-	BASF, 1965
	Dog	9000 mg/kg	CNS and cardiac depressant	+/-	Shideman, 1951
	Dog	4600-5500 mg/kg	Only LD50 reported	+/-	Stenger, 1972
	Cat	> 1840 mg/kg	Behavioural reversible changes	+/-	BASF, 1965

B.5.3 Irritation

In animal studies (rabbits), PGME was found to be slightly irritating to the skin and slightly irritating to the eye. PGME is not expected to be severely irritant for the respiratory tract. No classification is needed for irritation.

One study perfomed in human volunteers showed that PGME was moderately irritant at dose of 300 ppm for a short period of time. At 100 ppm no effects of irritation (objective) were seen. The value of 100 ppm will be taken into account in the risk characterisation for eye and upper respiratory tract irritation by inhalation.

B.5.4 Corrosivity

PGME is not a corrosive substance.

B.5.5 Sensitisation

PGME was found to be non-sensitizing in guinea pigs. PGME is not expected to be a respiratory sensitiser. No classification is needed for these end-points.

B.5.6 Repeated dose toxicity

There is no guideline study for oral or dermal repeated dose toxicity. There is no human data available.

In the majority of the studies, transient CNS depression was seen at doses of 3000 ppm leading to a NOAEL of 1000 ppm for this effect (acute effect). In rats evidence of specific male nephropathy was noticed in almost all studies, this effect is not relevant for human and will therefore not be taken into account for the risk assessment. The main toxicological effects noticed in rats were liver effects: increases in liver and relative liver weight, induction of hepatic enzyme and cellular proliferation. Concerning this effect, a NOAEC of 300 ppm (1122 mg/m3) is derived from a well performed 2-year rat study.

Table 5.2: Summary inhalation route.

Study	**Results**	**NOAEC**	**Validity**	**Reference**
Rat				
Wistar 6h/d 10 days 0 – 200 – 600 ppm	Only testes effects checked. No effects	NA	2	Doe, 1983

Study	Results	NOAEC	Validity	Reference
Fischer 344 9 exposures 0 – 300 – 1000 – 3000 ppm	CNS depression at 3000 ppm. No irreversible effects on organs	1000 ppm 3740 mg/m^3	1	Miller, 1981
Fischer 344 9 exposures in 11 days 0 - 3000 ppm	Sedation in treated group. Increase in relative liver weight. Slight increases of kidneys weights. Specific nephropathy in male.	-	2	Stott, 1992
5h/d 5d/w 2 weeks 2500 – 5000 – 10000 ppm	Reversible CNS depression at 5000 and 10000 ppm. Decrease growth rate was seen at 10000 ppm.	2500 ppm 9350 mg/m^3	2	Goldberg, 1964
Fischer 344 6h/d 5d/w 13 weeks 0 – 300 – 3000 ppm	Sedation at 3000 ppm. Male specific nephropathy at all doses.	300 ppm 1122 mg/m^3	1	Cieszlak, 1996
Fischer 344 6h/d 5d/w 13 weeks 0 – 300 – 1000 – 3000 ppm	CNS depression at 3000 ppm. Slight increase in liver weight and slight decrease in female body weight gain.	1000ppm 3740 mg/m^3	1	Landry, 1983
7h/d 5d/w 6 months	-	> 1500 ppm 5600 mg/m^3	3	Rowe, 1954
2-year study 0 – 300 – 1000 – 3000 ppm	Effects on liver from 1000 ppm. Specific kidneys effects on male rats	300 ppm 1122 mg/m^3	1	Cieszlak, 1998
Mouse				
B6C3F1 9 exposures 0 – 300 – 1000 – 3000 ppm	CNS depression at 3000 ppm. No irreversible effects on organs.	1000 ppm 3740 mg/m^3	1	Miller, 1981
B6C3F1	CNS depression in the treated group. Increase	< 3000 ppm < 11220	2	Stott, 1992

Study	Results	NOAEC	Validity	Reference
9 exposures in 11 days 0 - 3000 ppm	in relative liver weight and hepatocellular proliferation.	mg/m^3		
B6C3F1 6h/d 5d/w 13 weeks 0 – 300 – 1000 – 3000 ppm	CNS depression at 3000 ppm. Renal and hepatic cellular proliferation ar 3000 ppm. Increase hepatic enzymatic induction at 3000 ppm. Increased in liver weight in females at 3000 ppm.	1000 ppm 3740 mg/m^3	1	Cieszlak, 1998
2-year study 0 – 300 – 1000 – 3000 ppm	Increased mortality in males at 3000 ppm related to liver toxicity.	1000 ppm 3740 mg/m^3	1	Cieszlak, 1998
Rabbit				
3 –6 month 800 – 1500 – 3000 – 6000 ppm	Slight increases of liver weight in females and slight histological changes of the liver and lungs at 1500 and 3000 ppm.	800 ppm 3000 mg/m^3	3	Rowe, 1954
6h/d 5d/w 13 weeks 0 – 300 – 1000 – 3000 ppm	CNS depression at 3000 ppm. Slight increases of alkaline phosphatase at 3000 ppm..	1000 ppm 3740 mg/m^3	1	Landry, 1983
Guinea pig				
7h/d 5d/w 6 months 0 – 1500 – 3000 ppm	No effects seen.	3000 ppmp < 11220 mg/m^3	3	Rowe, 1954
Monkey				
7h/d 5d/w 6 months 0 – 800 – 1500 – 3000 ppm	No details available	800 ppm 3000 mg/m^3	3	Rowe, 1957

Validity

1: valid without restriction

2: valid with restriction

3: not valid or not assessable

Only two studies are available to assess effects of repeated exposure to PGME. The only systemic effect seen was narcosis from 3676 mg/kg and higher (moreover this effect can be considered as an acute effect). Slight inflammation was seen locally at doses < 1000 mg/kg. Based on the only reliable study a NOAEL of 1000 mg/kg will be taken into account for systemic effects by dermal route. The LOAEL for local effects is 1000 mg/kg.

Table 5.3: Summary of RDT dermal route

Study	**Results**	**NOAEL**	**Validity**	**Reference**
Rabbit				
5d/w 90 days 0 to 10 ml/kg	High doses (7 – 10 ml/kg) produced narcosis and mortality. Slight narcosis was seen from 4ml/kg.	2 ml/kg (about 1840 mg/kg)	3	Rowe, 1954
21 day (15 - application) 0 – 1000 mg/kg	No systemic effects at tested dose. Slight scaling and minimal inflammation was seen on the treated skin.	> 1000 mg/kg for systemic effects < 1000 mg/kg for local effects	2	Calhoun, 1984

Validity

1: valid without restriction

2: valid with restriction

3: not valid or not assessable

Only four studies were performed to assess the repeated dose toxicity properties of PGME by oral route. None was made according GLP and guidelines. Overall for oral route, a LOAEL of 460 mg/kg can be taken into account (from a rat and a dog study) based on slight CNS depression seen from this dose in rats and dogs (13-week study for rats and 14-week study for dogs) and a NOAEL of 919 mg/kg by oral route for systemic effects (hepatic effects).

Table 5.4: Summary RDT oral route

Study	Results	NOAEL	Validity	Reference
Rat				
CFE rats 13 week oral feed 460 – 919 – 1836 – 3672 mg/kg	CNS depression at all doses. Liver enlarged at doses > 919 mg/kg with cell necrosis. Kidneys effects at 3672 mg/kg	< 460 mg/kg	2	Stenger, 1972
35 days 0 – 92 – 276 – 919 – 2757 mg/kg	Reversible decrease in body weight gain at the high dose. At the higher dose, slight effects on the liver and kidneys were noted.	919 mg/kg	3	Rowe, 1954
Rabbit				
3 rabbits only one dose: 1840 mg/kr 9 treatments	Effects on erythrocytes and lymphocytes. One animal died.	< 1840 mg/kg	3	BASF, 1965
Dog				
5d/w 14 weeks 460 – 919 – 1836 – 3672 mg/kg oral feed	CNS depression. Kidney changes at highest dose.	< 460 mg/kg	2	Stenger, 1972

Animals exposed to PGME via inhalation and oral route have developed central nervous systems effects (sedation).

Hepatic mixed function oxidase activity and hepatocellular proliferation were increased at high doses, sometimes accompanied with mild degenerative changes or necrosis (in rare cases).

Minimal nephropathy in male rats was sometimes described with specific alpha-2-μ-globulin deposition in the kidney. Therefore, these renal effects are not relevant to humans.

By dermal route, local effects were reported at doses of about 1 g/kg (the only dose tested): scaling, minimal inflammation, and skin thickening. No systemic effects were reported at this level of dose leading to a NOAEL of 1000 mg/kg. The LOAEL for local effects was 1000 mg/kg/d.

By inhalation, a NOAEC of 300 ppm for liver effects is derived from a well performed 2-year rat study (6 h exposure for 5 days a week). By dermal route, a NOAEL of 1000 mg/kg was found for systemic effects based on a 21-day study in rabbits. By oral route, a LOAEL of 460 mg/kg can be taken into account for CNS effects in rats and dogs (13-week study for rats and 14-week study for dogs) and a NOAEL of 919 mg/kg by oral route for systemic effects (hepatic effects).

B.5.7 Mutagenicity

PGME was not mutagenic in bacteria (*Salmonella typhimurium* TA 1535, TA 1537, TA 1538, TA 98, and TA 100), *in vitro* tests on mammalian cells, or in one *in vivo* test on mice. The data available would indicate the PGME is not genotoxic.

B.5.8 Carcinogenicity

No human data available.

In a 2-year bioassay, no statistically significantly increases in tumors in any tissue (except kidney tumors in males) were observed in male and female rats exposed to PGME via inhalation (Cieszlak *et al.*, 1998a). The increase in kidney tumours was considered not relevant to humans since it is assumed to be due to a male rat specific mechanism.

There were no increases in tumors in any tissue in a 2-year study of male and female mice exposed to PGME via inhalation (Cieszlak *et al.*, 1998b).

PGME is not carcinogenic and that therefore, no Risk Assessment for this end-point is necessary.

B.5.9 Toxicity for reproduction

Fertility

Commercial PGME is a mixture of two isomers (α and β). The β-isomer is metabolized to 2-
methoxypropionic acid, a strongly suspected animal teratogen (Hellwig et al, 1994 – Merkle et al, 1987). Although commercially available PGME contains less than 0.5% of the β-isomer, the PGME tested in some animal studies described here was altered to contain approximately 2% of the β-isomer : Liberacki, 1997,

NOAELs observed in a two-generation reproductive study on exposure to PGME via inhalation were 300 ppm (1122 mg/m^3) for adult rats and 1,000 ppm (3740 mg/m^3) for offspring (Liberacki *et al.*, 1997, Carney *et al* 1999). Sedation and decreased body weight in adults was accompanied by lengthened estrous cycles, decreased fertility, decreased ovary weights and associated ovarian atrophy, reduced pup survival and litter size, slight delays in pubertal indices, and histological changes in the liver and thymus (in offspring) at the highest dose tested (3000 ppm). However, the nature of these effects and the close correlation with decreased maternal body weights suggest that these effects were secondary

to general toxicity and/or nutritional stress. For oral exposures, a NOAEL of 1% in drinking water in a two-generation mice reproduction study was reported (Chapin and Sloane, 1997). Reduced pup weights, and in the second generation reduced adult body weights, and a decrease in epidydimal and prostate weights was observed at the highest dose tested (2% in drinking water). In another study (Doe *et al*., 1983), male rats exposed to 200 or 600 ppm PGME via inhalation (6 hours/day for 10 days) showed no effects on the testes.

Effects on fertility were seen at relatively high doses in the presence of slight systemic toxicity. Based on effects seen on females at 3000 ppm in the 2-generation study, the most relevant NOAEC was 1000 ppm .

Development

In all studies, maternal toxicity was found at high doses (mainly CNS depression and decrease food consumption with decrease body weight gain). In fetuses, slight effects were seen: delayed ossification in some studies (sternebral or skull) but always in presence of maternal toxicity. No teratogenic effects were observed at doses up to 3,000 ppm by inhalation route or 1 ml/kg by oral route.

In the 2-generation studies, foetotoxic effects were seen concurrently with maternal toxicity (3000 ppm by inhalation in rats (11220 mg/m^3) and 2% in drinking water in mice.)

This kind of effects (delayed ossification) is often reported concurrently with the maternal effects described in the available studies. Due to the low toxicity of PGME and that no specific developmental effects were observed at relatively high dose without maternal toxicity, it is considered that developmental toxicity of PGME is of no concern.

B.5.10 Other effects

B.5.11 Derivation of DNEL(s)/DMEL(s) or other quantitative or qualitative measure for dose response

B.6 Human health hazard assessment of physico-chemical properties

This part has been agreed by TCNES based on the RAR finalised the 28th October 2008 [1].

B.6.1 Explosivity

PGME has no explosive properties.

B.6.2 Flammability

PGME is flammable (flash point is 32°C). Vapours can form flammable and explosive mixtures with air within the range of 1.7 to 11.5 % volume. Information on flammability and safety measures should be given on the label and the safety data sheet. There is at present no need for further information or risk reduction measures beyond those which are being applied already.

It is also noted that oxidation by air may involve peroxidation of the substance, which may increase explosive properties. A general warning to this effect is recommended. Use of antioxidants reduces the potential to peroxidation.

B.6.3 Oxidising properties

PGME has no oxidising properties.

B.7 Environmental hazard assessment

Agreed by TCNES based on the RAR [2] . For more details, please refer to this document.

B.7.1 Aquatic compartment (including sediment)

Table 7.1: Summary of aquatic PNEC

Compartment	**PNEC**
Aquatic compartment	10 mg/l
Saltwater	1 mg/l
Wet weight of sediment	9.04 mg/kg
Wet weight of marine sediment	0.904 mg/kg

B.7.2 Terrestrial compartment

No test on plants, earthworms or other soil-dwelling organisms is available. In the absence of any ecotoxicological data for soil-dwelling organisms, the $PNEC_{soil}$ may provisionally be calculated using the equilibrium partitioning method with the PNEC for aquatic compartment ($PNEC_{aqua}$) and the soil-water partition coefficient.
Thus, the $PNEC_{soil}$ value is of 2.18 mg/kg wet weight of soil.

B.7.3 Atmospheric compartment

No data is available. The $PNEC_{air}$ can not be determined.

B.7.4 Microbiological activity in sewage treatment systems

A NOEC $\geq$ 1,000 mg/l for sludge was determined from the respiration inhibition test (Klecka et al., 1985). The $PNEC_{STP}$ may then be calculated using this value and an assessment factor of 10 which gives a $PNEC_{STP}$ value of 100 mg/l for organisms of STP.

B.7.5 Non compartment specific effects relevant for the food chain (secondary poisoning)

PGME is not classified T+, T or Xn and its potential for bioaccumulation is very low.

B.8 PBT and vPvB assessment

PGME is not classified T+, T or Xn and its potential for bioaccumulation is very low. [2]

B.8.1 Assessment of PBT/vPvB properties – Comparison with criteria of Annex XIII

B.8.2 Emission characterisation

B.9 Exposure assessment

B.9.1 General discussion on releases and exposure

Humans may be exposed to PGME at workplace, via consumer products and indirectly via the environment (i.e. ingestion of surface water). The highest potential exposure is likely to occur during occupational exposure.

Workers and consumers are primarily exposed via inhalation and dermal routes. PGME is readily absorbed through the skin including absorption from direct contact with liquid or aerosol form or contact with vapours. Dermal exposure from direct contact with liquid PGME may contribute significantly to overall exposure, due to its relatively low vapour pressure (1.16 kPa at 20°C).

Exposure may occur during manufacture and use as intermediate in the chemical industry, and during formulation and use of products. PGME is a solvent used in many industrial activities or consumer applications. Over the past two decades, ethylene glycol methyl ether and ethylene glycol ethyl ether have progressively been replaced by propylene glycol derivatives. The main uses of PGME are in paints or surface coatings (solvent-based or water-based), followed by cleaners and printing inks. Other minor uses reported are solvent in the electronic industry, in cosmetics/personal care (capillary tinting, nail-varnish removers), leather finishing agents, adhesives, agricultural and oil field chemicals.

According to the SIDS initial assessment profile (2001), PGME is used in the manufacture of PGME acetate as well as in a wide variety of industrial and commercial products, including paints and varnishes (30% for surface coatings), printing inks (6%), cleaners (23%), adhesives and electronics (7%).

In the Swedish product register (KEMI, 2002), 906 products containing PGME (of which 250 were private household products) have been identified: 59 % are paints (or hardeners for paints), varnishes or adhesives, 9 % cleaning agents, 5 % dyestuffs and 5 % diluents.

In the Danish product register (Arbejdstilsynet, 2001), 3387 products containing PGME have been identified,. The most common uses were paints, lacquers and varnishes (74 %), solvents (4 %), cleaning/washing agents (5 %) and process regulators (4 %).

Other data extracted from the French product register SEPIA (INRS, 2003) showed that 243 products registered between 1997 and 2002 contained PGME. The main use category was: paints, varnishes and inks (45 %).

Dentan *et al*. (2000) analysed the chemicals registration database in Switzerland in order to identify users of PGME and potential exposure. In 1999, out of 150,000 products, 2,334 were found to contain PGME and most between 1% and 10% PGME. There was a great increase in the number of products declared between 1983 and 1991, which reflects the trend to replace certain ethylene glycol ethers by propylene glycol ethers. The most common uses were inks, paints and varnishes (50 %), solvents, diluents and pickling

solutions (13 %), cleaning agents (10 %), glues, mastics and jointings (5 %), auxiliary materials (5 %).

A more recent French survey on glycol ethers reported two other studies which provide additional information:

- A study from a French Union for Consumers (UFC “que choisir”, 2003) indicated that out of 17 window cleaners, 80% contained PGME, PGPE or PGBE without no other details. However, none of the 18 “multi-uses” house cleaners contained any glycol ethers.
- Another French study from CSTB (Scientific and Technical Center for Building) in 2006 showed that 50% of the cleaners/detergent bought in supermarket (the cheapest and the most expensive one of each category) produced glycol ethers such as PGME, PGPE, PGBE, EGBE, DGEE, EGPhE and EGME in emission measures without any other details.

B.9.2 Occupationnal exposure

B.9.2.1 Manufacture and use as intermediate

See 4.1.1.2.1 (Manufacture and use as intermediate) of the human health part of the EU-RAR (attached to annex XV dossier).

B.9.2.2 Formulation of products containing PGME

See 4.1.1.2.2 (Formulation of products containing PGME) of the human health part of the EU-RAR (attached to annex XV dossier).

B.9.2.3 Use of products containing PGME

See 4.1.1.2.3 (Use of products containing PGME) of the human health part of the EU-RAR (attached to annex XV dossier).

B.9.2.4 Summary of occupational exposure

For more details, see 4.1.1.2.4 of the human health part of the EU-RAR (attached to annex XV dossier).

Table 9.2: Summary of proposed reasonable worst case exposures

Scenario	8-hour TWA inhalation (mg/m^3)	External Dermal exposure (mg/day)
1 - Manufacture	2.7	42
2 - Formulation	87	3,000 (loading and filling)
3 - Use of products		
3.1 Coating/Painting*		
- industrial		
- Spraying	100	3,000
- Other works	61	360
- decorative	61	180
3.2 Cleaning		
- spraying	151	250
- wiping	151	1,000
3.3 Printing		
- silk screening	100	23
- flexography	100	168
- general printing	35	168

* The conclusions refer to solvent-based paints. Exposure from use of water-based paints (lower PGME content) would be much lower.

As pointed out in the report, dermal exposure may make a significant contribution to overall exposure and needs to be considered carefully. The estimates based on measured data from RISKOFDERM should be preferred to the EASE estimates as they represent real exposure situation and EASE is known to be a weak model for this purpose.

RISKOFDERM measured data are however overestimated, especially when measurements have been done with gloves and when they are based on the much less volatile DEGBE. The level of overestimation cannot be estimated but the uncertainty caused by the measurement method should be taken into account for risk characterisation in the evaluation of the MOS. This is particularly relevant for scenario 1 (formulation) and scenario 2 (painting).

B.9.3 Consumers exposure

See 4.1.1.3.1 (Exposure from uses) of the human health part of the EU-RAR (attached to annex XV dossier).

Table 9.3: Summary of proposed reasonable worst case exposures in the main scenarios

Scenario	Inhalation		Skin	Sum of exposures
	(mg/m3)	(mg/kg/d)	(mg/kg/d)	(mg/kg/d)
1. Indoor air	0.048	0.01		0.01
2. Aqueous paints and floor varnishes	61	20.3	7.7	28
3. house cleaners	330	1.5	9.8	11.3

B.9.4 Human exposed via the environment

See 4.1.1.4 of the human health part of the EU-RAR (attached in the annex XV dossier).

B.9.5 [Summary of] environmental exposure assessment

The concentrations calculated in intake media (drinking water, fish, plant roots and leaves, milk, meat, air) relating to the estimation of the indirect exposure of humans via the environment and the subsequent estimation of human intakes via different routes were evaluated in the RAR [1] with the corresponding total daily intakes. Both local and regional levels were taken into consideration and the estimation of local environmental exposures has been performed for all scenarios evaluated. Concerning the production step, only the worst case has been reported. All calculations have been performed using EUSES 2 and default parameters of this software have been used excepted a value of 30% for dermal absorption and a value of 100% for inhalation exposure and a body weight of 60 kg. The highest indirect exposure is estimated for the production : 0.526 $mg.kg^{-1}.day^{-1}$. It can also be noted that the highest exposures are to be expected through intake of drinking water, fish and plants (leaves and roots). Moreover, based on the regional concentrations, the total daily intake for humans is 3.7×10^{-4} $mg.kg^{-1}.day^{-1}$.

B.9.6 Combined human exposure assessment

Combined exposure was assessed only for workers and risk was identified for repeated toxicity for occupational combined exposure (see B.10.1.2b).

B.10 Risk characterisation

See 4.1.3 of the human health part of the EU-RAR (agreed by TCNES) attached to the annex XV dossier.

B.10.1 Human health

B.10.1.1 General aspects

Table 10.1: Summary of effects

Substance name	Inhalation (N(L)OAEL)	Dermal (N(L)OAEL)	Oral (N(L)OAEL)
Acute toxicity	< 6038 ppm (22.5 mg/l) (LD50) 750 ppm CNS depression in human	13g/kg (LD50: mortality) 1000 mg/kg	4016 mg/kg
Irritation / corrositivity	100 ppm (374 mg/m^3) for eye and upper respiratory tract irritation	NA	NA
Sensitization	NA	NA	NA
Repeated dose toxicity (local)	NA	< 1000 mg/kg	NA
Repeated dose toxicity (systemic)	1000 ppm (3740 mg/m^3) CNS depression 300 ppm (1122 mg/m^3) hepatic effects	> 1000 mg/kg	< 460 mg/kg (narcotic effects) 919 mg/kg (hepatic effects)
Mutagenicity	NA	NA	NA
Carcinogenicity	NA	NA	NA
Fertility impairment	1000 ppm (female) (3740 mg/m^3)	NA	NA
Developmental toxicity	NA	NA	NA

NA: not applicable

B.10.1.2 Workers

Conclusion iii applies to:

a. cleaning spraying and wiping (coating/painting) for eye and respiratory tract irritation

Table 10.2 : Risk characterisation for eye and respiratory tract irritation effects

Scenario	8-hour TWA inhalation (mg/m3)	MOS (minimal MOS=3)	Conclusion
Cleaning spraying and wiping	151 [NOAEC: 374 mg/m^3]	2.5	iii

b. formulation, coating-painting scenarios (industrial spraying), cleaning (spraying, wiping) and printing (silk screening, flexography) for repeated toxicity by combined exposure *(NOAEC = 1122 mg/m^3)*

Table 10.3 : Risk characterisation for repeated toxicity by combined exposure

Scenario		Internal dose after inhalation exposure (mg/kg) Y + Z*	Internal dose after dermal exposure to liquid PGME (mg/kg)	Total internal dose (inhalation + dermal combined exposure)	MOS (minimal MOS = 12.5)	Conclusion
Formulation		13.8	12.9	26.7	6.7	iii
Use of products	Coating/Painting					
	-industrial spraying	15.9	12.9	28.8	6.2	iii
	Cleaning					
	spraying	24	1.08	25.08	7.1	iii
	wiping	24	4.29	28.29	6.3	iii
	3.3 Printing					
	- Silk screening	15.9	0.096	16	11.1	iii
	- flexography	15.9	0.72	16.6	10.7	iii

* Y (inhalation internal dose) = X (value of the 8-hour TWA inhalation (mg/m^3)) x 10 m^3 (inhaled air during a workday) x 1 (100 % absorption by inhalation) / 70 (mean bw of a worker)
* Z = 0.10/0.90 x Y = 0.11 Y (dermal absorption of vapour PGME could count for 10 % of the internal dose of PGME)
* For dermal exposure internal dose is calculated for a 70 kg bw worker with a percentage of absorption of 30 % (liquid PGME, worst case)

c. formulation and industrial spraying (coating/painting) for local effects after repeated dermal exposure

Table 10.4 : Risk characterisation for local effects

Scenario	Estimated Skin exposure mg/day worst case (mg/kg bw/d)	MOS (Minimal MOS = 37.5)	Conclusion
2 - Formulation	3,000 (43)	23	iii
3 - Use of products			
3.1 Coating/Painting			
- industrial			
- Spraying	3000 (43)	23	iii

These MOS are calculated using worst case scenarios for dermal exposure and without use of PPE. In the RAR, it is specified that it might be considered that using PPE conclusion ii could be reached instead for all scenarios.

For all other scenarios and end-points there is no concern (**Conclusion ii).**

B.10.1.2 Consumers

Conclusion iii is reached for eye and respiratory tract irritation for house cleaners scenario

Table 10.6: MOS and conclusion for eye and respiratory tract irritation

Scenario	Inhalation (mg/m3)	MOS (minimal MOS = 3)	Conclusion
3. House cleaners	330	1.1	iii

Conclusion ii is reached for all other consumers' scenarios concerning all other toxicological end-points.

The consumer exposure to PGME has been estimated with the model provided in the Technical Guidance Document. Recent new data not provided in the RAR about dermal and inhalation exposure of consumers using house cleaners could mitigate the conclusion.
The following results summarised in the table 10.7 were published in 2008 by AFSSET (French Agency for Environmental and Occupational Health Safety) and are extracted from a study about VOC emissions measurement and particularly PGME by different types of products used in indoor environments. This work have been carried out by a French Scientific and Technical Center for Building [CSTB 2006]. Thirty-two among 7 categories of products (air freshener, floor cleaners, window cleaners, impregnated wipes floor

cleaners, stain removers, dust removers, toilets cleaners) were tested in realistic conditions of use and ventilation in an experimental house or in emission chamber. The products were selected by retaining the most expensive and cheapest product categories products identified in several shops signs of large retailers. PGME has been measured in two categories of products (floor carpet cleaner and floor cleaner).

Table 9.4: Emission measurement of PGME from household cleaner

Type of Product	**Concentration of PGME measured (mg/m^3) after:**			
	0-30 min	30-60 min	60-90 min	90-120 min
Floor carpet cleaner	109	91	57	41
Floor cleaner (undiluted)	43	14	3	0,7

Results show that the model lead to a probable slight overestimation of the consumer inhalation exposure.

B.10.1.3 Indirect exposure tu humans via environment

Conclusion (ii) "There is at present no need for further information and/or testing and or risk reduction measures beyond those applied already" for all endpoints in relation to local and regional exposure.

B.10.2 Environment

The risk assessment does not cover the use of PGME in oilfield chemicals or its use in oil spill dispersants (see Section 3.1.2.1.3 and 3.1.2.1.4 of EU-RAR [2]) and lead to the following conclusions:

Conclusions to the risk assessment for the aquatic compartment:

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

Conclusions to the risk assessment for the terrestrial compartment:

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

Conclusions to the risk assessment for the atmospheric compartment:

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

Conclusions to the risk assessment for secondary poisoning:

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

B.11 Summary on hazard and risk

PGME has a very low acute toxicity by all routes of exposure. Only very slight signs of irritation were observed for skin, eyes or respiratory tract. PGME is not sensitising to animals, and there are no human data available.

Repeated dose toxicity show few hepatic effects after inhalation exposure and by oral route CNS reversible effects were seen at all tested doses. PGME is not a mutagenic substance and no carcinogenicity is expected according to the data available. Effects on fertility were seen at relatively high doses in the presence of marked systemic toxicity. Slight developmental effects of PGME were observed in pups of treated dams. These effects were seen at high doses and always in presence of maternal toxicity.

Workers

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

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) 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 ii is reached for all other scenarios**.**

Consumers

Conclusion iii is reached for eye and respiratory tract irritation for house cleaners scenario..

Conclusion ii is reached for all other consumers scenarios concerning all other toxicological end-points.

Humans exposed via the environment

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.

This conclusion applies for all endpoints in relation to local and regional exposure.

Human health (risks from physico-chemical properties)

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.

B.12 Summary of existing legal requirements and risk management measures proposed

B.12.1 For workers

PGME is listed in annex I according to the 19th ATP to Directive 67/548/EEC under index number: 603-064-00-3 as R10; S2-24. Based on the effects assessment provided in the RAR, it has been proposed and agreed by the TCNES to complete the classification and labelling by adding R67 risk phrase in addition to R10.

As a result of its classification as hazardous substance, PGME is subject to general regulations concerning its supply and handling.

Safety Data Sheets:

In accordance with article 31 (title IV) of Regulation (EC) No 1907/2006, the supplier of a substance or a preparation that meets the criteria for classification as dangerous in accordance with Directives 67/548/EEC or 1999/45/EC shall provide the recipient of the substance or preparation with a safety data sheet compiled in accordance with Annex II.

The information system for hazardous substances and preparations in the form of labelling and the safety data sheets is considered sufficient in principle to provide the user with sufficient information for the selection of suitable occupational safety measures. The SDS should contain all relevant information from the risk assessment report.

Occupational safety and health regulations:

At the European level, the following directives are primarily applicable as general regulations for occupational safety and health of workers in the production and use of PGME:

- 98/24/EC on the protection of workers from the risk related to exposure to chemical agent at work.
- 89/656/EEC on the use of personal protective equipment

Only limited knowledge is available about the extent to which the EU member states have in each case transposed these basic requirements into national law.

Occupational exposure Limits:

OELs apply to workplace air concentrations of chemicals. They are normally intended to protect workers against short-term adverse effects (irritation, acute Central Nervous System (CNS) effects) or long-term effects (e.g. on liver, lungs, kidneys, or chronic CNS effects) after months or years of exposure. When applicable, a "short-term exposure limit" (STEL) may be proposed or imposed to protect against the former effects, and/or a "time-weighted average" (TWA) for the latter. The short term value ordinarily refers to a 15 minutes or so duration, the second to a shift (generally considered as an 8-hour shift).

In accordance to Commission Directive 2000/39/EC of 8 June 2000 establishing a first list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work, table 12.1 presents the OELs recommended for PGME in various countries. They are provided for information and are not an indication of the level of control of exposure achieved in practice in workplaces.

Table 9.1: Occupational Exposure Limit values for PGME

Country	8-hr TWA		STEL, 15 min	
	mg/m^3	ppm	mg/m^3	ppm
EU[a,b]	**375**	**100**	**568**	**150**
Austria[b]	187	50	187[1]	50[1]
Belgium	374	100	561	150
Denmark	185	50	370[1]	100[1]
Finland	370	100	560	150
France[b]	375	100	568	150
Germany	370	100	740[1]	200[1]
Ireland[b]	360	100	1,080	300
Italy	369	100	553	150
Netherlands	375	100	563[1]	

Norway[b]	180	50	-	-
Spain[b]	374	100	748	200
Sweden[b]	190	50	300	75
Switzerland	360	100	720	200
UK[b]	375	100	748	200
USA (ACGIH)	369	100	553	150
USA (NIOSH)	370	100	553	150

a: Directive 2000/39/CE of 8 June 2000
b: with skin notation
1: http://bgia-online.hvbg.be/LIMITVALUE

In France, a recent survey on glycol ethers exposure assessment indicates that all the exposures to PGME are much below the exposure limits: for the years 2000 to 2006, the COLCHIC database collected 615 personal atmospheric sampling results of PGME. The arithmetic mean value of 60 to 480 minutes samplings was 10.04 mg/m^3 (median 3 mg/m^3, range 0.1-206 mg/m^3, 95th percentile 39 mg/m^3; see also database extract reported in the RAR in 4.1.1.2.3 to see the decreasing tendency). There is few data which could help to extrapolate these results to other EU countries where PGME is also produced or used.

Personal protective equipment:

According to community Legislation, workers have to be provided with suitable Personal Protection Equipment (PPE) if their health is at risk due to exposure against chemicals. PPE that protects against the risks of PGME is available and has to be indicated in the SDS.
On account of probable irritation effects of PGME, the use of suitable protective equipment is in general widely accepted, if dermal exposure cannot be excluded by other technical or organisational measures. French investigations within the framework of the assessment of occupational exposure to glycol ethers also noted that individual protections are often made available instead of collective measures to protect the workers both from dirt associated with the activities and contact with toxic products. Finally, the skin notation provided with the EU-OELs should improve the acceptance of gloves.

Considering the uncertainties highlighted along the risk assessment the legislation for workers' protection currently in force at Community level is generally considered to give an adequate framework to limit the risks of the substance to the extent needed and shall apply.

No data regarding the number of workers exposed are available but due to the wide range of products containing PGME, it is assumed that a large number of workers in many professional sectors in several member states of EU may be exposed daily or occasionally. Few data are available to extrapolate most of information on workers protection collected in France to other countries of the community. ECHA should ask the forum to work on that matter.

According to the results or in order to adopt a more protective strategy, the Commission should request the SCOEL to reconsider the OELs values adopted few years ago in the light of the risk assessment report.

There are no further risks reduction measures proposed but, in order to ensure an effective enforcement of the current occupational regulation and to improve the enforcement of the actual legislation and the protection of the workers, there is a need to make the classification proposed by the TCNES legally binding (i.e. PGME should be added to the annex I of the directive 67/548/EEC). France could then propose an annex XV dossier for PGME in the year 2009.

B.12.2 For consumers

Based on the effects assessment provided in the RAR, it has been proposed and agreed by the TCNES to complete the classification and labelling by adding R67 risk phrase in addition to R10.

Consequently, based on Annex V of Directive 99/45/EC on classification, packaging and labelling of dangerous preparations, when a preparation contains one or more substances assigned the phrase R67, the label of the preparation must carry the wording: “vapours may cause drowsiness and dizziness” when the total concentration of these substances present in the preparation is equal to or higher than 15 %, unless:

- the preparation is already classified with phrases R20, R23, R26, R68/20, R39/23 or R39/26,
- or the preparation is in a package not exceeding 125 ml.

It is likely that household cleaners producers would voluntary limit the concentration of PGME in their products to max 15% to avoid the mandatory risk phrase “vapours may cause drowsiness and dizziness” which is particularly stressful since it call to mind a risk of loss of consciousness. Considering the effects observed and the uncertainties highlighted for the consumer exposure in the RAR (model, maximum percentage of PGME), and considering the toxicological profile of most of the potential substitutes for PGME, it seems neither appropriate nor proportional to propose a restriction.

However, PGME can be found in a wide variety of commercial products all over Europe, including aqueous paints, floor varnishes, cleaning agents and detergents, and nail varnish remover. Furthermore, recent data shows that there is an important increase in the production and use of PGME mostly due to the substitution of series-E glycol ethers by series-P.

In order to help reducing consumer’s exposure to PGME and to improve the communication of the effects and risks associated to products containing PGME in an harmonised manner around the EU community, there is a need to make the classification proposed by the TCNES legally binding (i.e. PGME should be added to the annex I of the directive 67/548/EEC). France could then propose an annex XV dossier for PGME in the year 2009.

C. AVAILABLE INFORMATION ON ALTERNATIVES

To be filed in REACH-IT and used when needed: detailed information on glycol ethers and their alternative can be found in the survey joined to the dossier [3].

G. STAKEHOLDER CONSULTATION

Stakeholders have been regularly consulted in the frame of the different studies conducted in France.

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ANNEXES