European Union Risk Assessment Report

1-METHOXYPROPAN-2-OL ACETATE

CAS No: 108-65-6

EINECS No: 203-603-9

RISK ASSESSMENT

Final human health risk assessment

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Final human health draft

October 2008

France

Rapporteur for the risk assessment of 1-methoxy-2-propanol acetate is the Ministry of Spatial Planning and the Environment as well as The Ministry of Employment and Social Affairs in co-operation with the Ministry of Public Health. Responsible for the risk assessment and subsequently for the contents of this report is the rapporteur.

The scientific work on this report has been prepared by the National Institute for Research and Security (INRS) as well as the National Institute for Industrial Environment and Risks (INERIS), by order of the rapporteur.

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Foreword

This Draft Risk assessment Report is carried out in accordance with Council Regulation (EEC) 793/93[1] on the evaluation and control of the risks of "existing" substances. "Existing" substances are chemical substances in use within the European Community before September 1981 and listed in the European Inventory of Existing Commercial Chemical Substances. Regulation 793/93 provides a systematic framework for the evaluation of the risks to human health and the environment of these substances if they are produced or imported into the Community in volumes above 10 tonnes per year.

There are four overall stages in the Regulation for reducing the risks: data collection, priority setting, risk assessment and risk reduction. Data provided by Industry are used by Member States and the Commission services to determine the priority of the substances which need to be assessed. For each substance on a priority list, a Member State volunteers to act as "Rapporteur", undertaking the in-depth Risk Assessment and recommending a strategy to limit the risks of exposure to the substance, if necessary.

The methods for carrying out an in-depth Risk Assessment at Community level are laid down in Commission Regulation (EC) 1488/94[2], which is supported by a technical guidance document[3]. Normally, the "Rapporteur" and individual companies producing, importing and/or using the chemicals work closely together to develop a draft Risk Assessment Report, which is then presented at a Meeting of Member State technical experts for endorsement. The Risk Assessment Report is then peer-reviewed by the Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE) which gives its opinion to the European Commission on the quality of the risk assessment.

This Draft Risk Assessment Report is currently under discussion in the Competent Group of Member State experts with the aim of reaching consensus. During the course of these discussions, the scientific interpretation of the underlying scientific information may change, more information may be included and even the conclusions reached in this draft may change. The Competent Group of Member State experts seek as wide a distribution of these drafts as possible, in order to assure as complete and accurate an information basis as possible. The information contained in this Draft Risk Assessment Report does not, therefore, necessarily provide a sufficient basis for decision making regarding the hazards, exposures or the risks associated with the priority substance.

This Draft Risk Assessment Report is the responsibility of the Member State rapporteur. In order to avoid possible misinterpretations or misuse of the findings in this draft, anyone wishing to cite or quote this report is advised to contact the Member State rapporteur beforehand.

[1] O.J. No L 084, 05/04/199 p.0001 – 0075

[2] O.J. No L 161, 29/06/1994 p. 0003 – 0011

[3] Technical Guidance Document, Part I – V, ISBN 92-827-801 [1234]

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0 OVERALL RESULTS OF THE RISK ASSESSMENT[4]

[Note: In the final report, chapters 0 and 5 should be as close as possible to the OJ]

CAS Number: 108-65-6
EINECS Number: 203-603-9
IUPAC Name: 1-methoxypropan-2-ol acetate

Human health

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

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

Consumers

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

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

4 Conclusion (i) There is a need for further information and/or testing.
Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

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.

Human health (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.

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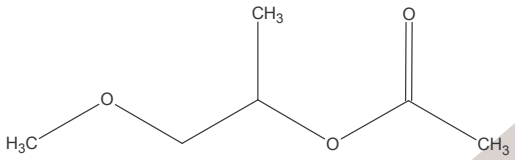
1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS Number: 108-65-6
EINECS Number: 203-539-1
IUPAC Name: 2-methoxy-1-methylethyl acetate
Molecular formula: $C_6H_{12}O_3$
Structural formula: $CH_3O\text{-}CH_2\text{-}CH(CH_3)\text{-}O\text{-}COCH_3$



Molecular weight: 132.16 $g.mol^{-1}$
Synonyms: 1-methoxy 2-acetoxy propane; 1-methoxy 2-propyl acetate; 1-methoxy-2-propanol acetate; 1-methoxy-2-propyl acetate; 2-acetoxy-1-methoxypropane; 2-propanol, 1-methoxy-, acetate; acetate de l'ether methylique de propylene glycol; acetate de 2-methoxy-1-methylethyle; Dowanol PMA glycol ether acetate; methoxy propyl acetate; propylene glycol methyl ether acetate; propylene glycol monomethyl ether acetate; PGMEA; PGMA

In the risk assessment, the name PGMA will be used for the substance, as this is the most common name.

1.2 PURITY/IMPURITIES, ADDITIVES

The commercially supplied product is usually a mixture of substances: 2-methoxy-1-methylethyl acetate (PGMA, CAS n°108-65-6) and 2-methoxypropyl acetate (CAS n°70657-70-4).

PGMA is the main compound, totalizing more than 99.5 % of the product with less than 0.5 % of 2-methoxypropyl acetate, considered as an impurity.

No additive is contained in the marketed product.

1.3 PHYSICO-CHEMICAL PROPERTIES

At ambiant temperature and pressure, PGMA is a colorless liquid with an ether-like odour.

1.3.1 Melting point

The melting point of PGMA ranges from –88°C to < -67°C (BP, 2000; Dow France, 2001). A producer used as ASTM D-97 method reporting a result of –65°C (SHELL, 2000). The test reports are not available.

A median value of –76°C has been calculated with the above data. This value will be used for the risk assessment.

1.3.2 Boiling point

The boiling point of PGMA ranges from 140 to 146°C (BP, 2000; Dow France, 2001; LYONDELL, 1999). A producer used an ASTM D-1078 method reporting values ranging from 143 to 149°C (SHELL, 2000). And another producer used a DIN 53 171 method reporting values ranging from 145 to 147°C (BASF, 2001). However, the test reports are not available.

A median value of 146°C has been calculated using the above data. This value will be used for the risk assessment.

1.3.3 Relative density

The density of PGMA ranges from 0.964 to 0.97 g/cm^3 at 20°C (Dow France, 2001; SHELL, 2000). At 25°C, the density of PGMA is 0.96 g/cm^3 (LYONDELL, 1999). A producer used an DIN-51 757 method reporting values ranging from 0.965 to 0.97 g/cm^3 at 20 °C (BASF, 2001). However, the test reports are not available.

A median value of 0.967 g/cm^3 has been calculated at 20°C using the above data. This value will be used for the risk assessment.

1.3.4 Vapour pressure

The vapour pressure of PGMA ranges from 3.37 to 4.9 hPa at 20°C (BASF, 2001; BP, 2000; Dow France, 2001; SHELL, 2000). At 25°C, the value of 5.07 hPa is reported (LYONDELL, 1999). No test report is available.

A median value of 4.2 hPa at 20°C has been calculated using the above data. At 25°C, the value of 5.93 hPa has been calculated. This last value will be used for the risk assessment.

1.3.5 Surface tension

A surface tension of 30.4 mN/m is reported at 20°C by one producer. The concentration of the substance in water was unknown (BP, 1998).

Surface active properties can be assumed for glycol ethers. The values reported in the literature for PGMA tend to indicate that this substance is a surface active reagent even if no indication has been found about the concentration of the substance during the test quoted above. Indeed, OECD guideline n°115 suggests that surface tension measurements should be performed using a concentration of 1 g/L for soluble substances.

The fact that glycol ethers show surface active properties could thus lead to the disturbance of analytical method employed to measure some physico-chemical characteristics of glycol ethers.

However, there is a difference between the surface activity of traditional surfactants and substances that can reduce the surface activity of solutions like PGMA. What is observed with

the glycol ethers during the surface tension measurements is the typical non ideal behaviour of a mixture of a water miscible solvent such as methanol and ethanol. The reason for the observed relationship between surface tension and concentration is the disruption of the hydrogen bonding of the water causing non-linear behaviour of the surface tension against the concentration. In this case the substance is not migrating to the surface; it is not acting in the traditional surface active manner. Therefore it would not affect the measurements of the physical chemical properties. One should also noticed that glycol ethers do not form micelles. They are fully miscible with water and form clear solutions.

Furthermore, considering the other properties of this substance (PGMA is highly miscible in water, hydrosphere is the preferential target of PGMA in the environment : 90%), surface active properties of PGMA will not be considered in this assessment. At worst, this could lead to an overestimation of the risks calculated for the aquatic compartment.

1.3.6 Water solubility

PGMA is very soluble in water.

Chemicals Evaluation and Research Institute (1998) measured the solubility in water using flask method (OECD GL 105). The test report is not available, but it was validated by the Japanese authorities within the OECD SIDS activities. A value above 100 g/l was measured at 25°C. This value will be used in the risk assessment.

1.3.7 Henry's law constant

Staples and Davies (2002) calculated Henry's law constant from aqueous solubility and vapor pressure using a solubility of 160 g/l and a vapor pressure of 517 Pa. Value was 0.43 $Pa.m^3/mol$.

The Henry's law constant was also estimated using a structure activity relationship HenryWin v3.10 (US EPA and Syracuse Research Corporation, 2001). Calculated values ranged from 0.059 $Pa.m^3/mol$ (group method) to 0.367 $Pa.m^3/mol$ (bond method).

The Henry's law constant can be calculate using selected values of this report. The resulting value is 0.78 $Pa.m^3/mol$.

According to these values, PGMA is stable in water.

An average value of 0.41 $Pa.m^3/mol$ has been calculated using the above data. This value will be used for the risk assessment.

1.3.8 Partition coefficient octanol water

A log P_{OW} value was determined by reverse-phase HPLC by Pearson (1986). The HPLC system used was a reverse-phase C_{18}-coated silica gel column with a mobile phase of 3 volumes methanol and 1 volume water (final pH 6.8). Samples of an approximate 1 mg/ml solution in the above mobile phase were injected and the emergence of the material observed using refractive index detection. From the retention time of the peak the log P_{OW} value was determined. Fourteen reference substances with log P_{OW} ranging from 0.94 to 5.88 were used

to generate a linear relationship between the retention time and log P_{OW} and to determine log P_{OW} of PGMA.

Pearson (1986) also calculated a log P_{OW} value from chemical structure using the fragment addition method of Hansch and Leo (1979).

The log Pow values of PGMA determined by HPLC and the fragment-addition method were respectively 1.2 and < 1.

Gonsior (1990) also estimated a log P_{OW} value using the Pomona-Med Chem Structural fragment method. A value of 0.56 was calculated.

Using a QSAR (US EPA and Syracuse Research Corporation, 2001: KOWWIN v1.66), a log P_{OW} of 0.52 was estimated.

BASF (2001) reported a partition coefficient octanol water for PGMA of 0.43. No test report is available.

Chemicals Evaluation and Research Institute (1998) measured the partition coefficient between octanol and water using the flask-shaking method (OECD GL 107). The test report is not available, but it was validated by the Japanese authorities within the OECD SIDS activities. A value of 0.36 at 25°C was measured.

The partition coefficient octanol water of 0.36 will be chosen for the risk assessment as it was obtained by an experimental method.

1.3.9 Other physical-chemical properties

1.3.9.1 Flash point

The flash point of PGMA ranges from 42°C to 50°C (BASF, 2001; BP, 2000; Dow France, 2001; LYONDELL, 1999; SHELL, 2000). The test reports are not available.

An average value of 45.8°C has been calculated using the above data. This value will be used for the risk assessment.

1.3.9.2 Autoflammability

Decomposition of PGMA starts at temperature ranging from 272°C to 354°C (BASF, 2001; BP, 2000; Dow France, 2001; LYONDELL, 1999; SHELL, 2000). The test reports are not available.

An average value of 317.8°C was calculated using the above data. This value will be used for the risk assessment.

1.3.10 Summary

Table 1.1 Summary of physico-chemical properties

Property	Value
Physical state	Liquid
Melting point	-76°C
Boiling point	146°C
Relative density	0.967 at 20°C
Vapour pressure	5.93 hPa at 25°C
Water solubility	100 g/l at 25°C
Partition coefficient n-octanol/water (log value)	0.36
Flash point	45.8°C
Autoflammability	317.8°C
Henry's constant	0.41 Pa.m^3/mol

1.4 CLASSIFICATION

1.4.1 Current classification

R10
Xi; R36

S2-25

1.4.2 Proposed classification

R10

2 GENERAL INFORMATION ON EXPOSURE

3 ENVIRONMENT

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

4.1.1.1 General discussion

Humans may be exposed to PGMA 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. PGMA is readily absorbed through the skin including absorption from direct contact with liquid or aerosol form or contact with vapours. Because this compound has a relatively low vapour pressure (0.49 kPa at 20°C), dermal exposure from direct contact with the liquid may be predominant or contribute significantly to overall exposure.

Exposure may occur during manufacture and during formulation and use of products. PGMA is a solvent used in many industrial activities or consumer applications. Over the past decades ethylene glycol methyl ether and ethylene glycol ethyl ether acetates, have progressively been replaced by propylene glycol derivatives. The main use of PGMA is in paints or surface coatings (solvent-based or water-based). Other uses reported are solvent in the electronic industry, in the chemical industry, in inks, cleaners, and adhesives,.

In the Swedish product register (KEMI, 2002), 1097 products containing PGMA (of which 126 were private household products) have been identified : 66 % are paints (or hardeners for paints), varnishes or adhesives , 8 % diluents, 1 % solvents and 1 % cleaning agents.

In the Danish product register (Arbejdstilsynet, 2001), 1758 products containing PGMA have been identified, of which 83 were private household products. The most common uses were paints and varnishes (48 %), solvents (11 %), process regulators (11 %), adhesives/binding agents (6 %) and cleaning/washing agents (3 %).

Other data extracted from the French product register SEPIA (INRS, 2002) showed that 265 products registered between 1997 and 2002 contained PGMA. The main use category was: paints, varnishes and inks (79 %).

The distribution of concentration intervals in the main type of products is presented in the tables 4.1 and 4.2.

Table 4.1: Concentration of PGMA in the main use categories in the Danish product register (Arbejdstilsynet, 2001)

Content %	Cleaning agents	Solvents	Paints	Process regulators	Adhesives
[0-1]	5	7	341	25	36
]1-5]	4	6	189	28	21
]5-10]	12	14	133	37	12
]10-20]	8	29	116	76	15
]20-50]	14	91	45	23	14
]50-80]	3	24	12	5	3
]80-100]	4	27	-		

Table 4.2: Concentration of PGMA in the main use categories in the French product register SEPIA (INRS, 2002)

Concentration (%)	Paints, varnishes and inks	Metallurgical and mechanical sectors products	Cleaning products
[0-1]	29	1	-
]1-5]	63	5	-
]5-10]	38	1	-
]10-20]	40	4	2
]20-50]	5	1	2
]50-100]	1	-	1

4.1.1.2 Occupational exposure

Definitions and sources

In this document, unless otherwise stated, the term exposure is used to denote external personal exposure as measured or otherwise, assessed without taking into account the attenuating effect of any personal protective equipment (PPE) which might have been worn. This definition permits the effects of controls other than PPE to be assessed and avoids the considerable uncertainty associated with attempting to precisely quantify the attenuation of exposure brought about by the proper use of PPE. Furthermore, inappropriate use of gloves may even increase dermal uptake.

The worst-case estimates generated in this exposure assessment are considered to be reasonable worst-case estimates, as they describe high-end or maximum exposures in feasible but not unrealistic situations. They are not intended to account for extreme or unusual use scenarios. The majority of exposures are expected to be well below these estimates.

Air sampling data are presented in this section from a number of sources and have been tabulated, where practicable. There is in general little or no information on the activities carried out while the sampling was running, the concentration of PGMA in the products, the control measures, and other important matters, such as sampling strategy and measurement methods, mean and 90^{th} or 95^{th} percentile of results; this is most often a serious difficulty for interpreting the data correctly.

Measured exposure data are compared with that predicted from the EASE (Estimation and Assessment of Substance Exposure) model version 2. EASE is a general purpose predictive model for workplace exposure assessments. It is an electronic, knowledge based, expert system which is used where measured exposure data is limited or not available. The model is in widespread use across the European Union for the occupational exposure assessment of new and existing substances.

No measured dermal exposure data are available for PGMA. A few results have been measured with relevant analogous substances. They will be considered together with modelling to predict occupational dermal exposure to PGMA. Many of the references stress the importance of dermal exposure, particularly during use of products. All sections on dermal exposure deal with liquid exposure.

All models are based upon assumptions. Their outputs are at best approximate and may be wrong. EASE is only intended to give generalised exposure data; it predicts inhalation exposure as ranges for concentrations for continuous exposure at the process under consideration. Dermal exposure is provided by EASE as the quantity of a product adhering to the skin due to a task (evaporation of the product is not taken into account).

Since glycol ethers can be absorbed by all routes, biological monitoring represents the best approach for assessing total exposure. However no biomonitoring study are available for PGMA.

In the present assessment inhalation exposures are expressed in mg/m^3 or ppm. All ppm have been converted to mg/m^3 using the following approximation:

$mg\ PGMA/m^3 = ppm \times 132.16/24.05 = ppm \times 5.49$

Routes of exposure and relevant scenarios

The major occupational routes of exposure to PGMA 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 PGMA, its use as a processing solvent in the chemical industry or during the formulation and use of PGMA containing products.

Occupational exposure assessment will be carried out through three main categories of scenarios:

(a) the manufacture of PGMA and its use as a processing solvent,

(b) the formulation of products containing PGMA,

(c) the use of products containing PGMA.

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.

Number of workers exposed

No data are available but due to the wide range of products containing PGMA, it is assumed that there are a large number of workers in many professional sectors who may be exposed daily or occasionally.

Occupational exposure limits (OELs)

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).

Table 4.3 presents the OELs recommended for PGMA 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 4.3: Occupational Exposure Limit values for PGMA

Country	8-hr TWA		STEL, 15 min	
	mg/m^3	ppm	mg/m^3	ppm
Austria	110	20	220	40
Denmark	110	20	-	-
Germany	110	20	240	80
Norway[a]	110	20	-	-
Switzerland[a]	110	20	220	40

Nota a: with skin notation

4.1.1.2.1 Scenario 1 : Manufacture and use as a processing solvent

This scenario includes all activities concerning the production and use of PGMA as a processing solvent. Although the data mainly refer to the manufacture of PGMA, exposure is expected to be similar during its use in the chemical synthesis industry. Both processes take place in closed systems under strict control. A few people are exposed during these activities. In the EU there are three sites producing PGMA.

PGMA is manufactured in a closed system, either continuously or on a campaign basis. Exposure during transfer to tankers or drums is generally minimized by the use of automated filling, where the operator is segregated from the area during transfer, and the use of local exhaust ventilation. Accidental exposure may occur when the process is breached or when spills occur. Exposure may also occur during maintenance and cleaning activities. However the purging of plant and equipment is generally standard practice.

Inhalation exposure

Measured data

Airborne measurements were provided by an EU manufacturer of PGMA in the framework of this assessment: 89 measurements made in the production plant between 1979 and 1997 result in exposure ranging from < 0.05 mg/m^3 to 23 mg/m^3, with an average of 0.22 mg/m^3 and a 90th percentile of 3.52 mg/m^3. Results are presented in table 4.4. No more details are available (probably personal exposure).

Table 4.4: Inhalation exposure measurements in an EU plant (1979-1997)

Type of processing/workplace	No of results	Range (mg/m^3)	Average (mg/m^3)
All	89	0.05-23	1.21
Internal users	26	0.05-23	1.1
Production	11	0.05-1.8	0.33
Storage/filling	8	0.05-0.88	0.22
Laboratory	20	0.05-3.52	0.55
Maintenance	22	0.22-15.4	2.64
Disposal	2	0.38-0.60	-

Modelled data

The EASE model used to predict exposure during production in closed system with full containment provides an exposure estimate of 0-0.1 ppm (0-0.55 mg/m^3). If the system is breached in some activities (like maintenance, sampling, cleaning, filling), concentrations could be in the range of 0.5-1 ppm (2.7-5.5 mg/m^3) (non dispersive use, low tendency to become airborne, presence of LEV).

Summary/statement of the exposure level

Limited monitoring data are available for production and use of PGMA in the chemical synthesis industry. Due to automated processes for feeding reactors and for drum and tanker filling as well, inhalation exposure is likely to be low in most situations (< 1 mg/m^3).

Taking into account the available measured data and the EASE estimates, it is proposed to adopt the value of 3.5 mg/m^3 (90th percentile of measured data) as a reasonable worst-case TWA atmospheric concentration for these activities.

Dermal exposure

Due to the enclosure of the process and control measures taken to minimize skin contact, for example, during transfer to tankers, dermal exposure at the plant is incidental and therefore likely to be low. The main source of potential exposure is during maintenance activities.

Incidental contact with the liquid seems appropriate for this scenario because exposure will be occasional (not daily) and intermittent contact would probably overestimate the exposure. The EASE model estimated a dermal exposure in the range of 0-0.1 mg/cm^2/day (non dispersive use with direct handling and incidental contact). Assuming exposed skin surface area is 420 cm^2 (palms of hands), maximum external dermal exposure would be 42 mg/day. This exposure will be mitigated by the use of suitable gloves.

4.1.1.2.2 Scenario 2 : Formulation of products containing PGMA

During the formulation of products containing PGMA, workers may be exposed during pre-weighing before mixing, during transfer to the mixing tank, during mixing and during the filling of containers with products. The whole operation is generally carried out at room temperature. Because of the similarity of scenarios, it will be assumed that exposure during formulation is the same whatever the final use of products is.

Exposure strongly depends on the process, which may be enclosed or relatively open. When the transfer of PGMA to the mixing vessel is carried out in a sealed system, potential exposure will be minimal, but when the operator adds the raw materials directly by drum to the mixing tank, exposure may be greater due to possible splashing and vapour and/or aerosol generation.

Exposure will also strongly depend on the quantities handled, the concentration in the products and the duration and frequency of exposure.

During preweighing and transfer to the mixing tank, workers are potentially exposed to pure PGMA, they are exposed to a more dilute form during filling. However the frequency and duration of exposure may be greater. As operators may be involved in both mixing and filling, assessment of exposure is for the formulation process as a whole.

Quite a high number of workers are likely to be exposed during formulation of products. An enquiry was recently conducted by CEPE (European council of the paint, printing and artists' colours industry) on the industrial uses of 4 glycol ethers in paints or inks manufacturing industries. For PGMA, 109 answers were received from all over Europe, 62 users and 47 non-users. They comprise both multinationals and small or medium size enterprises from most of the EU countries. The number of workers exposed was indicated by 43 user companies out of the 76, the answers were in the range of 1 to 250 and represent a total number of 1563 workers (CEPE, 2002).

Information about exposure frequency and duration has also been recently collected in the CEPE enquiry (see table 4.5).

Table 4.5: Exposure frequency and duration in paints and inks manufacturing industries (CEPE, 2002)

	Exposure in days/year (42 answers)	Exposure in hours/day (41 answers)
Arithmetic mean	147	4.5
Median	190	4.0
Range	3-365	0.5-8

Inhalation exposure

Measured data

There are very few measured data published for assessment of exposure during formulation :

- Exposure of 17 workers in a varnish production facility was examined. The workers (n=12) in the production area were found to be exposed to PGMA at an average concentration of 2.8 ppm (15.4 mg/m^3); individual exposures ranged from < 0.1-13.8 ppm (< 0.55-75.8 mg/m^3). The exposure of the workers in the store (n=3) and in the laboratory (n=2) were too low to measure (Angerer *et al*., 1990).

- Between 1988 and 1993, INRS (Vincent *et al*., 1996) performed a large study of occupational exposure to glycol ethers by atmospheric and biological monitoring. During this study, personal exposure of 248 workers in 5 factories of the paint manufacturing industry were measured (328 air samples). The study was performed when the use of ethylene glycol ethers were still widespread compared to propylene glycol ethers. PGMA was not frequently detected and the majority of samples was under the limit of detection of 0.1 ppm (0.55 mg/m^3). The highest measured exposure was 0.2 ppm (1.10 mg/m^3).

In the inquiry of CEPE (2002), 15 facilities out of the 62 PGMA users who answered the questionnaire said they performed workplace monitoring (30 replied negatively to the question while the others did not answer at all). In several instances, the companies specified too low concentration to measure. Two companies gave a quantitative information (4.5 mg/m^3 and 1.8 mg/m^3) but no data are available to the context of this results.

Information from database

In the German MEGA database, 438 exposure measurements have been registered between 1992 and 1997, and 509 between 1998 and 2001, which were mainly obtained in the paint formulation industry. The results (measurement values with an exposure duration ≥ 1 hour and a sampling duration ≥ 1 hour converted to 8-hour weighted averages) are presented in tables 4.6 and 4.7. The measurements were mainly obtained during mixing and filling of PGMA and during the cleaning of equipment or containers.

When possible, a distinction is made on the basis of whether or not control measures (LEV) were taken. In this regard, the results present an apparent paradox that the workplaces with LEV frequently do not exhibit lower exposures than those without LEV and the exposures may even be higher. Technical measures are mostly taken in place where the situation may result in a higher release of vapours, for instance when large quantities of substance are handled or when process occurs at high temperature. By contrast, the release is comparatively low during use of small

quantities or processing at ambient temperature. In most cases, control measures create a situation where the exposure level inworkplaces with large release approximately reaches the level of workplaces with only low release but without control measures.

Table 4.6: Personal inhalation exposure (8-hr TWA) in the MEGA database, 1992-1997 (BGAA, 2001)

Paint production activity	No of results	No of companies	50% value (mg/m^3)	90 % value (mg/m^3)	95 % value (mg/m^3)
Raw PGMA handling, mixing and filling	323	75	5	25	35
- without LEV	128	47	5	19	28
- with LEV	181	49	5	27	39
Cleaning of containers	115	64	7	28	50
- without LEV	25	20	11	43	163
- with LEV	82	46	6	27	39

Table 4.7: Personal inhalation exposure (8-hr TWA) in the MEGA database, 1998-2001 (BGAA, 2001)

Paint production activity	No of results	No of companies	50% value (mg/m^3)	90 % value (mg/m^3)	95 % value (mg/m^3)
Raw PGMA handling, mixing and filling	374	103	a	23.60	32.60
- without LEV	113	52	a	22.40	26.70
- with LEV	258	81	a	24	36.80
Cleaning of containers	135	69	a	38.50	62.50
- without LEV	28	17	a	41	53
- with LEV	100	52	a	24	50

a = measurement value < analytical determination limit

Modelled data

Using the EASE model (non dispersive use, low tendency to become airborne), the exposure estimate would be in the range of 0.5-1 ppm (2.74-5.49 mg/m^3) with LEV and 10-20 ppm (54.9-109.8 mg/m^3) in case of direct handling with dilution ventilation.

Summary/statement of the exposure level

Published data are too limited to derive a worst case exposure level. Based on the highest 90th percentile of the MEGA database values, the worst case inhalation exposure during formulation of products is assumed to be 43 mg/m^3. Typical exposure levels are probably much lower.

Information presented in table 4.5 shows that frequency and duration of exposure may considerably vary. A continuous exposure for full shift (8 hours per day) will be assumed although the data suggests that this is unlikely to be a daily exposure.

Dermal exposure

Measurements

In a study performed by TNO (Riskofderm, 2002a and Gijsbers J.H.J. *et al*., 2004), a part of the Riskofderm project, potential hand exposure to an analogous but much less volatile glycol ether, DEGBE (2-(2-butoxyethoxy)ethanol, vapour pressure 2.7 Pa at 20°C) was measured during loading (typically at the beginning of the formulation process, handled product is the substance, short task duration ranged between 1 and 15 minutes) and during filling (typically at the end of the formulation process, handled product is the formulation, task duration ranged between 22 and 125 minutes). The measurements were made using cotton sampling gloves which were worn over new protective gloves, where present. Exposure was mainly due to exposure on the hands. The most important source of variability was due to between-company variability, rather than to either between-worker or within-worker variability. Results (given in DEGBE and product) are presented in table 4.8.

Table 4.8. Results of measurements of potential hand exposure to DEGBE in loading mixers and filling containers with products containing DEGBE (after Riskofderm, 2002a and Gijsbers *et al*., 2004)

Exposure to DEGBE or product	*N*	*Range (mg)*	*AM (mg)*	*GM (mg)*	*GSD (mg)*	*AM (µg/cm²/min)*	*GM (µg/cm²/min)*	*GSD (µg/cm²/min)*
Loading (pure DEGBE)								
Hands DEGBE	28	0.28-28300.0	3313.6	218.9	19.9	727.4	52.9	17.2
Hands Product*	28	0.31-27745.1	3215.0	217.0	19.3	708.8	52.4	16.7
Filling (all data)								
Hands DEGBE	30	0.062 – 19000.0	1955.8	35.9	42.0	45.1	0.75	42.6
Hands Product*	30	4.1 – 18269.2	2726.6	555.4	9.4	58.5	11.5	9.6
Filling (only products < 10% DEGBE); data not published, but calculated from original data								
Hands Product*	21	4.1-11146	1216	249	8.5	15	4.1	7.6

N = number of measurements
AM = arithmetic average
GM = geometric average
GSD = geometric standard deviation)
*recalculated towards the full product by dividing the value measured for DEGBE by the fraction of DEGBE as analysed in the product

The 90th percentile from the measured data for loading was approximately 11,000 mg on 840 cm^2 (expressed as total product), approximately 11,100 mg on 840 cm^2 for filling (all products, including (almost pure) DEGBE) and approximately 3300 for filling of products containing less than 10% of DEGBE (not published data, derived from original data). This value would lead to a level of 330 for DEGBE if the percentage of DEGBE would be 10%. It appears that the situations with handling (almost) pure products lead to higher exposure levels. That can be caused by the fact that products with small percentages of DEGBE, such as paints can be packaged in cans by highly automated equipment, while (almost) pure DEGBE is often packaged in larger containers with more handling of the container by the workers.

Modelling

Considering the process and the tasks where exposure may occur, SIDS (1996) retained intermittent contact time of 20 % of the working day with a 1000 cm^2 skin area exposed (a hand and a forearm).

Taking into account the same assumption, the EASE model estimates a dermal exposure in the range of 0.1-1 mg/cm^2/day (non dispersive use with direct handling and intermittent contact). Assuming exposed skin surface area is 420 cm^2 (for consistency with other EU occupational risk assessments and default assumptions recommended in table 3 of Appendix I of the Technical Guidance), maximum external exposure would be:

- 42-420 mg/day for loading (pure substance)
- 21-210 mg/day for filling (assuming 50% PGMA in the product)

Assessment

Dermal exposure can occur during part of the working day during loading of mixers (short periods, up to approximately 20 minutes) and during packaging of products containing PGMA (up to 120 minutes per day). Measured data for this scenario for PGMA are not available. Data from DEGBE for similar processes may be relevant. The measured values, using cotton gloves as samplers, for DEGBE are generally high compared to the estimates by EASE. Geometric mean exposure levels to products, for situations where formulations were made, so excluding the filling of (almost pure) DEGBE, were in the order of 200-250 mg and the 90th percentile was in the order of 3300 for filling of products with less than 10% DEGBE and 11,000 mg for loading of DEGBE into mixers, both on 840 cm^2. The measured data for DEGBE may be an overestimate of potential dermal exposure for PGMA for two reasons. Firstly, the measurement method may have led to overestimation of dermal exposure, because cotton gloves are considered to retain more liquid than the skin would do. Secondly, PGMA is much more volatile than DEGBE and therefore, more of the substance may evaporate from the skin and not be available for uptake. The effect of both factors is difficult to estimate.

For the purpose of determining the evaporation time, the following equation can be used (TGD Appendix I.E):

$T(s)= (mRT/M\beta pA)K$

This equation leads for PGMA to an estimate of evaporation time of 32 minutes, with the following input values: m = 10 000 mg, R = 8.134 J.K^{-1}.mol^{-1}, T = 305 Kelvin, K = 3.6 * 10^4, M = 132.16, β = 8.7 m.h^{-1} (default), p = 490 Pa, A = 840 cm^2). This indicates that in approximately 32 minutes all PGMA would be evaporated from the skin. For comparison, the same calculation with DEGBE (vapour pressure = 2.7 Pa) leads to an evaporation time of more than 100 hours.

Different evaluations may be made using data from the RiskofDerm study for DEGBE (Gijsbers *et al.*, 2004), i.e. for loading:

0.709	x	1.00	x	840	x	6	=	3,570 mg
(mg/cm².min, A.M.)		(100% DEGBE)		(cm² for both hands)		(min, A.M.)		

using arithmetic mean (A.M.) data,
OR, using geometric mean data (and in this context maximum duration for filling):

0.0524	x	1.00	x	840	x	15	=	660 mg
(mg/cm².min, G.M.)		(100% DEGBE)		(cm² for both hands)		(min)		

The first calculation probably gives an overestimate, since it uses arithmetic means (which gives a strong weight to high values), and the second an underestimate (the geometric mean giving a strong weight to low values). So an intermediate value should be given preference.
In the case of EGBE, a chemical with physico-chemical properties more similar to PGMA than DEGBE, using data obtained from biomonitoring, it was estimated that the skin load might be around 500 mg/day; taking into account that "individual mean dermal exposure levels were on average within a 4-fold range" (Marquart *et al.*, 2006), a reasonable worst case skin exposure was

then re-evaluated as 2,000 mg/day, which is in-between the preceding evaluations but may still be slightly overestimated due to the greater volatility of PGMA.

As it is difficult to characterize overestimation due to the greater volatility of PGMA, it is proposed to use an exposure of 2000 mg/day for loading.

Similar evaluations may be made for filling (with an added multiplicative factor of 0.5 corresponding to an estimated concentration of 50%), which give 1000 mg/day.

If, on a worst case basis, a same worker is assumed to be in charge of both tasks, he then could be exposed to the sum of these assessments, i.e. 3,000 mg/day.

Dermal exposure may be lower if suitable gloves are worn.

4.1.1.2.3 Scenario 3 : Use of products containing PGMA

PGMA is used in a wide variety of products. The following scenarios are considered as representative:

- use of paints and coatings
- use of printing inks.

Cleaning related to painting and printing activities are included in these scenarios.

Measured exposure levels in general

From 1987 to 1998, the French COLCHIC database collected 10,593 personal sampling results of glycol ethers for 602 facilities (Vincent, 1999). PGMA was found 1761 times; the arithmetic atmospheric mean value of the 60 to 480 minutes samplings (455 results) was 16.4 mg/m^3 (median 2.1 mg/m^3; range 0.1-561 mg/m^3; 95th percentile 79 mg/m^3). Breakdown of exposure by industrial sectors is presented in table 4.9.

For the years 1999 to 2002, the COLCHIC database collected 399 personal atmospheric sampling results of PGMA. The arithmetic mean value of 60 to 480 minutes samplings was found 21.6 mg/m^3 (median 3.4 mg/m^3, range 0.1-966 mg/m^3, 95th percentile 136 mg/m^3) (Vincent, 2003).

Table 4.9: Personal inhalation exposure in the COLCHIC database, years 1987-1998, breakdown by industrial sectors (Vincent, 1999).

INDUSTRIAL SECTOR	No of samples	Arithmetic mean (mg/m^3)	Median. (mg/m^3)	Range (mg/m^3)	95th percentile (mg/m^3)
Wood and wood articles carving	12	9.8	8	2-29	29
Printing industry	110	8	4	0.2-140	33.3
Chemical industry	113	23.9	4	0.1-550	126
Rubber and plastics	64	7.2	2	0.1-54.7	34
Ore and metal treatment	22	0.1	0.1	0.1-1.2	0.3
Metal finishing	93	4.2	2	0.1-52	13
Electrical engineering	5	15.9	-	0.1-28	-
Communication equipment	3	10.6	-	3-17.4	-
Medical, optical and precision instruments	52	6.5	6	0.5-15	14
Automotive industry	6	16	-	0.5-49	-
Transport equipment production	3	70.7	-	1.5-209	-
Furniture manufacture	72	6.6	2	0.1-60.1	28

- **Scenario 3-1: Painting/Surface coating**

PGMA is used as a solvent in paints and surface coatings. It is its main application and due to the high volume used, a large number of workers are potentially exposed.

The answers related to concentration of PGMA in products, collected in the paint formulating industry by CEPE (2002) are presented in table 4.10. Taking into account this data together with the information collected in European products registers (tables 4.1 and 4.2), a worst case PGMA content of 30 % in industrial paints and 10 % in decorative paints will be assumed in this assessment. Therefore the conclusions in this section refer to solvent-based paints. Exposure from use of water-based paints (lower PGMA content) would be much lower.

Table 4.10: Contents of PGMA in paints (CEPE, 2002)

	Industrial paints		Decorative paints	
	Water-based	Solvent-based	Water-based	Solvent-based
Number of answers	7	43	3	8
Arithmetic mean	1.5 %	11.3 %	-	3.7 %
Median	0.3 %	7 %	-	2.5 %
Range	0.3-5 %	0.4-53 %	1-3 %	0.01-11 %

Coatings and paints are applied by spraying, rolling, brushing or dipping. Application techniques inventoried in the CEPE enquiry are presented in table 4.11 (CEPE, 2002):

Table 4.11: Relative frequencies of application techniques in painting/surface coating (CEPE, 2002)

Application technique	No of mentions
Spray	38
Roll	22
Brush	25
Dipping	5

Inhalation exposure

Measured data

In the INRS study performed between 1998 and 1993 (Vincent *et al*., 1996), occupational exposure was measured for a battery of glycols ethers, including PGMA. The results obtained for PGMA during painting or coating activities are summarised in table 4.12.

Table 4.12: Personal inhalation exposure (8 hr-TWA) during painting (Vincent *et al.*, 1996)

Activity	No of samples	Mean (mg/m^3)	Range (mg/m^3)
New car painting	39	2.74	<0.55-15.4
Car repainting	38	<0.55	<0.55-1.65
Aircraft repainting		105	78-160
Coil coating	261	0.55	<0.55—5.49
Metal frame painting	50	1.10	<0.55-15.4
Printed circuit board manufacture	57	<0.55	<0.55-5.49
Plastic painting	79	0.55	<0.55-11

Information from database

Exposure measurements (sampling period 60-480 minutes) registered between 1987 and 1998 in the COLCHIC database were analysed by Vincent (1999). Results related to painting and coating are presented in table 4.13:

Table 4.13: Personal inhalation exposure in painting activities in the COLCHIC database, years 1987-1998 (Vincent, 1999)

Type of work	No of samples	Mean (mg/m3)	Range (mg/m3)	Median (mg/m3)	95th percentile (mg/m3)
Pneumatic spraying of paint or varnish	90	8	0.5-60.1	4	31
Varnishing (curtain)	36	4.5	0.1.31	1.1	17.4
Brush or roll coating of paint or varnish	2	26.5	26-27	-	-

In the German MEGA database, 786 exposure measurements have been registered between 1992 and 1997, 1418 between 1998 and 2001, which were obtained during application of paints or coatings. The results (measurement values with an exposure duration ≥ 1 hour and a sampling duration ≥ 1 hour converted to 8-hour weighted averages) are presented in table 4.14 and 4.15. When possible, a distinction is made on the basis of whether or not control measures (LEV) were taken (see comments in scenario 2).

Table 4.14: Personal exposure measurements (8-hr TWA) in the MEGA database, 1992-1997 (BGAA, 2001)

Type of company/working area	No of results	No of companies	50% value (mg/m3)	90 % value (mg/m3)	95 % value (mg/m3)
Painting,brush and roller application, filling work	121	69	3	18	34
- without LEV	78	45	3	19	45
- with LEV	37	21	3	10	11
Spraying (compressed air, airless, airmix)	665	345	6	35	56
- without LEV					
- with LEV	81	49	6	56	92
	551	289	6	30	48

Table 4.15: Personal exposure measurements (8-hr TWA) in the MEGA database, 1998-2001 (BGAA, 2001)

Type of company/working area	No of results	No of companies	50% value (mg/m^3)	90 % value (mg/m^3)	95 % value (mg/m^3)
Painting,brush and roller application, filling work	139	68	a	48.20	75.05
- without LEV	66	33	a	71.20	102.40
- with LEV	58	31	a	16.80	42.10
Spraying (compressed air, airless, airmix)	804	362	a	22	36.80
- without LEV					
- with LEV	136	65	a	21.80	33.80
	611	284	a	21.90	36.45
Surface coating, mechanical					
- without LEV	203	97	a	16.70	28.70
- with LEV	89	43	a	13.10	21.10
	100	51	a	20.00	34.00
Surface coating, general					
- without LEV	133	69	a	29.70	45.40
- with LEV	47	24	a	15.00	17.30
	73	42	a	34.00	71.70

Nota a : measurement value < analytical determination limit

Modelled data

Exposure to vapours during the use of paints or surface coatings is estimated by EASE to be in the following range 100-140 ppm (549-769 mg/m^3) for wide dispersive, low tendency to become airborne, direct handling and dilution ventilation. This estimation is not suitable for spraying.

The model overestimates exposure levels, particularly because of non-consideration of the content of PGME in the mixtures. The estimates cannot be corrected for the partial vapour pressure because the composition of the formulations is not known. A simple approach based on a reduction of the exposure by a factor equivalent to the PGMA concentration in the mixtures (up to 30 % for industrial paints and 10 % for decorative paints) would lead to exposure levels of 165-231 mg/m^3 for industrial paints and 55-77 mg/m^3 for decorative paints. However the validity of these estimates is rather questionable.

Summary/statement of the exposure level

Exposure to PGMA during painting may be extremely variable, due to differences in frequency and duration of use, concentration of PGMA in the paint, method of application and precautions taken during use. To some extent, this variation is reflected in the atmospheric monitoring data available for PGMA during painting and surface treatment.

Although the spraying method of application would potentially increase exposure, it is proposed in a first approach to take for risk characterisation the same worst case inhalation exposure for all application techniques: 71 mg/m^3 based on the highest 90^{th} of the MEGA database values (1998-2001).

Dermal exposure

Measurements

In a study performed by TNO (Riskofderm, 2002a and Gijsbers J.H.J. *et al*., 2004), a part of the Riskofderm project, potential hand exposure to an analogous but less volatile glycol ether DEGBE (2-(2-butoxyethoxy)ethanol) was measured during indoors application of paint by brushing over of periods of 57-149 minutes (arithmetic mean 74 min). The sampling was ended when the painters (who usually painted for most of the working day) took a break for coffee or lunch, resulting in the measurement durations mentioned. The measurements were made using cotton sampling gloves which were worn over new protective gloves, where present. The amount of used product was between 0.5 and 2.5 litre (AM 1.2 litre) and the paint contained between 0.4 and 3.2 % DEGBE (AM 2 %). The treated area during measurements was between 2 and 15 m^2 (AM 6.4 m^2). Exposure was mainly due to exposure on the hands. Results (given in DEGBE and product) are presented in table 4.16.

Table 4.16 Dermal exposure rates during brushing (Gijsbers J.H.J. *et al*., 2004)

Hands exposure	N	W	Range (mg)	AM (mg)	GM (mg)	GSD (mg)	AM[c] (µg/cm²/min)	GM[c] (µg/cm²/min)	GSD[c] (µg/cm²/min)
- DEGBE	36	18	0.19-33.0	6.5	2.8	4	0.091	0.045	3.6
- product	24[a]	13	11.3-733.3	170.5	98.4	3	2.8	1.7	2.9

N, number of measurements; W, number of workers involved

AM, arithmetic mean; GM, geometric mean; GSD, geometric standard deviation

Nota a : for 12 of the measurements, exposure to product could not be calculated due to contamination of samples by other sources of DEGBE.

Nota c : a surface area of 820 cm^2 was assumed for the hands exposure

The 90th percentile of the measured exposure levels was approximately 400 mg product (unpublished data, derived from original data).

No measurements for dermal exposure in spray painting of PGMA or other direct analogues (e.g. other glycol ethers) are available. A number of dermal exposure data sets is available for other spray applications. Exposure to a non-volatile pigment was measured in car painting. Dermal exposure to the hands, expressed as total formulation, was between 2 and 211 mg (n = 30), with a median of 41 mg. Amount of product used was up to 1.5 kg in an average duration of 16 minutes (Riskofderm 2002b, Delgado *et al.,* 2004). Exposure to another non-volatile pigment was measured in marine anti-fouling painting. Dermal exposure to the hands, expressed as total formulation was between 286 and 27,000 mg (n = 24) for sampling periods of 1 to 3 hours. In this period 40 to 140 litres of paint were sprayed. Exposure was not only to workers actually doing spray painting, but also to auxiliary workers (so-called linesmen) assisting the spray painters. There was no difference in exposure between the two jobs. (Riskofderm 2002c, Hughson *et al.*, 2004). Spray application of a cleaning agent containing DEGBE was measured 12 times in the food industry. Duration of measurements ranged between 6 and 18 minutes. The in-use concentration of DEGBE was between 0.007 and 1.1%. The total amount of diluted product used was between 16.5 and 97.2 L. Dermal exposure to the hands, expressed as total formulation, was between 37 and 1974 mg (Riskofderm, 2003a). The 90th percentiles of these three data sets were respectively approximately 100, 13,600 and 1000 mg per measurement period (unpublished data, derived from original data). Older data are reported in the TGD, where for spray painting on large surface areas a reasonable worst case value of 10 000 mg product per day (on 840 cm^2) is given (Appendix I.E).

Modelling

For tasks as brushing and rolling, assuming wide dispersive use, direct handling and intermittent contact, the EASE model estimates a dermal exposure in the range of 1-5 mg of product/cm^2/day. For spraying, assuming an extensive contact leads to a dermal exposure range of 5-15 mg product/cm^2/day.;The estimation is made from a formulation containing up to 30 % of PGMA (industrial paint) and a formulation containing up to 10 % of PGMA (decorative paint) and an exposed skin surface area of 840 cm^2 (two hands). This leads to estimated external dermal exposures of :

- 252-1260mg/day for industrial painting (excluding spray application)
- 1260-3780 mg/day for industrial spray painting
- 84-420 mg/day for decorative painting.

Assessment

Skin contact due to manual transfer of liquids, spray application and brushing, rolling and cleaning is to be expected. In several of the available references, the importance of skin exposure is stressed.

The preference should be given to measured data, although there are difficulties in interpreting the Riskofderm data. Compared to the estimates by EASE, they may be closer to reality.

In the TNO study, cotton sample gloves can retain more material than skin leads to overestimation of exposure. The size of this possible overestimation is difficult to estimate. It can be expected that this overestimation is smaller when more viscous paints are used than when less viscous pure product is used. The fact that workers (except for breaks) may almost continuously do the same tasks suggests that the task based exposures should be extrapolated to a full work shift. Whereas extrapolation is clearly not valid for high (product) exposures, due to saturation of the surface of the skin, this is not so much of a problem with lower task exposure levels. Given the fact that painters spend part of their working period in preparation, moving between rooms, cleaning up the material and other non-painting tasks, the exposure period for painting can be estimated to be up to 6 hours. Based on the 90th percentile of the measured data (400 mg product in 2 hours), linear extrapolation to 6 hours of work and an assumed percentage of 30 % (industrial paint) or 10 % PGMA (decorative paint), the exposure value to be used in risk characterisation is estimated as 400*3*0.3 = 360 mg or 400*3*0.1 = 120 mg PGMA per day for brushing and rolling of industrial or decorative paints.

Using the RiskofDerm data (Gijsbers *et al.*, 2004), hand exposure in brushing activities may be assessed (product, geometric mean, maximum time) as:

0.0017	x	0.30	x	840	x	140	= 60 mg/day
(mg/cm².min)		(30% PGME)		(cm², both hands)		(min/day)	

OR (arithmetic mean, mean time):

0.0028	x	0.30	x	840	x	74	= 52 mg/day
(mg/cm².min)		(30% PGME)		(cm², both hands)		(min/day)	

These evaluations are underestimates due to the fact that “if measurement times were up to 139 min, painters were painting during most of their working day” (Gijsbers *et al.*, 2004). If the time taken into account is re-evaluated in both calculations at 360 min (i.e. 6 hours) they become respectively 154 or 254 mg/day, which is consistent with what is proposed above.

The exposure levels from industrial spray application apparently depend on the scale of application, as well as on control measures in use. Without further information, it is assumed that large scale application with limited exposure control can be done with paints containing up to 30% PGMA. The measured values over short periods cannot be extrapolated towards longer periods, because this

would lead to oversaturation of the skin. Therefore, a reasonable worst case exposure level of 10,000 mg product per day is assumed, based on the levels mentioned in the TGD and the measurements by Hughson *et al.* (2004). This leads to an estimated exposure to PGMA of 3000 mg on 840 cm^2. Because PGMA is much more volatile than the measured substances, this may be an overestimation. Also, if less large scale tasks are done, the exposure levels may be substantially lower. These uncertainties should be taken into account in the evaluation of the MOS.

Dermal exposure may be lower if suitable gloves are worn.

- **Scenario 3-2**: **Printing**

PGMA is used as a solvent in printing inks, particularly silk-screen inks used by professional trades. However there is a trend from solvent based inks to UV curing inks that contain no solvents.

Limited information have been collected in the enquiry recently performed in the ink formulating industry by CEPE (2002), only 4 answers were obtained in relation with the PGMA content in printing inks. They indicated content from 7 % up to 22 % in water-borne inks and 1.5-2 % in solvent-borne inks. Other data recently provided by one of the main producer of screen printing in the EU indicate that typical percentages of glycol ethers range from 2 to 35 % in screen printing inks (BP 2002). Taking into account all this data, typical maximum contents of 35 % PGMA in silk-screen inks and 20 % in others will be assumed in this assessment.

Inhalation exposure

Measured data

In the INRS study performed between 1998 and 1993 (Vincent *et al*., 1996), occupational exposure was measured for a battery of glycols ethers, including PGMA. The results obtained for PGMA during printing activities are summarised in table 4.16bis.

Table 4.16bis: Personal inhalation exposure (8 hr-TWA) during printing (Vincent *et al*., 1996)

Activity	No of samples	Mean (mg/m^3)	Range (mg/m^3)
Silk screening	295	1.65	< 0.55-16.5
Tampography	84	1.10	< 0.55-13.2

Auffarth *et al*. (1998) measured personal exposure in the screen-printing activity; measurement time was at least 1 hour. For 4 samples (hand printing), PGMA had a median of 10.0 mg/m^3 (range 3.5-22.6 mg/m^3). More samples (21) were available with a semi-automatic printing process; median and range were 5.7 mg/m^3 and 2.5-12 mg/m^3. With further automation (3/4), median and range were 6.8 mg/m^3 and 1.4-22.1 mg/m^3; with complete automation, median and range were 4.9 mg/m^3 and 3.2-10.4 mg/m^3.

Laitinen (1998) also found PGMA in the screen-printing industry, the mean atmospheric value being 8 ppm (44 mg/m^3), and short-term concentrations being 22 ppm (121 mg/m^3; semi-automated printing) and 95 ppm (522 mg/m^3; screen washing).

In the paints and lacquers industry in Poland, Wesolowski and Gromiec (1997) found PGMA in 7 personal samples (on a total of 179 samples of at least 6 hour duration) in 5 plants, with an arithmetic mean concentration of 3.8 mg/m^3 (range 0.0-25.7 mg/m^3).

Limited exposure measurements made in 2001 and provided by one of the main producer of screen printing inks in the EU have been presented by industry (BP, 2002). Printers are exposed 1-8 hours per day but 2-3 hours is the typical length time when workers are exposed to solvents. Nearly all operations use LEV as well as general ventilation. PGMA was detected in 72 samples amongst 161. The results are presented in table 4.17. The figures represent TWA over 2-3 hours.

Table 4.17: Personal air measurements (3-hr TWA) during screen printing (BP, 2002)

Activity	No of results	Mean (mg/m^3)	Maximum (mg/m^3)	5-95 % percentile (mg/m^3)
Print shop	59	2.2	21.4	0.1-9.2
Reclaim	11	2.4	15.5	0.1-9.9
Ink store	2	0.2	0.2	-

Information in database

Referring to the already cited French COLCHIC database (Vincent, 1999), 110 atmospheric personal samplings have been made between 1987 and 1998 in the printing industry, resulting in an arithmetic mean concentration of 8 mg/m^3 (range 0.2-140 mg/m^3; median 4 mg/m^3; 95^{th} percentile 33.3 mg/m^3). Results for specified activity are presented in table 4.18.

Table 4.18: Personal exposure in printing activities in the COLCHIC database, years 1987-1998 (Vincent, 1999)

Activity	Nb of results	Mean (mg/m^3)	Range (mg/m^3)	Median (mg/m^3)	95^{th} percentile (mg/m^3)
Screen printing	122	6	0.1.54.7	3.1	25
Screen washing	18	16.1	0.3-140	6.4	140
Offset printing	17	4.9	0.1-42	0.8	42
Cleaning	3	7.9	2.3-19	-	-
Flexography	15	12.7	0.5-44	1	44
Heliogravure	5	2.4	0.5-4	-	-

In the German MEGA database, 439 exposure measurements have been registered between 1992 and 2001, which were obtained during printing, mainly during screen printing. The results (measurement values with an exposure duration ≥ 1 hour and a sampling duration ≥ 1 hour converted to 8-hour weighted averages) are presented in table 4.19. When possible, a distinction is made on the basis of whether or not control measures (LEV) were taken (see comments in scenario 2).

Table 4.19: Personal inhalation exposure (8-hr TWA) during printing in the MEGA database, 1992-1997 (BGAA, 2001)

Period/working area type	No of results	No of companies	50% value (mg/m^3)	90 % value (mg/m^3)	95 % value (mg/m^3)
1992-1997	340	163	3	20	29
- without LEV	171	88	4	22	36
- with LEV	161	80	3	19	25
1998-2001	99	48	a	17.30	38.00
- without LEV	42	25	a	23.40	38.00
- with LEV	47	25	a	12.00	14.65

Modelled data

Exposure to vapours during printing is estimated by EASE to be in the range of 10-20 ppm (37.4-74.8 mg/m^3) for non dispersive use, direct handling with dilution ventilation.

The model overestimates exposure levels, particularly because of non-consideration of the content of PGMA in the products. The estimates cannot be corrected for the partial vapour pressure because the composition of the formulations is not known. A simple approach based on a reduction of the exposure by a factor equivalent to the PGMA concentration in the mixture (35 % for silk screen inks and 20 % for others) would lead to exposure levels of:

- 13.1-26.2 mg/m3 for silk screening
- 7.5-15 mg/m3 for general printing.

However the validity of these estimates is rather questionable.

Summary/statement of the exposure level

As can be seen from these relatively limited data and as was predictable in view of the variety in conditions of use and substance concentration in the product used, measured concentrations in air at the working place are highly variable depending the process and activities.

The highest exposure levels are likely to occur during screen printing. In the COLCHIC data; 95th percentiles of measured concentrations range from 25 to 140 mg/m^3. More recent results collected in the MEGA database are markedly lower (95th percentile range: 38 mg/m^3, 90th percentile range: 23 mg/m^3). A reasonable worst-case inhalation exposure of 40 mg/m^3 is proposed for these activities.

Lower exposure levels are measured for other activities. Mainly based on the highest 95th percentile COLCHIC data, a worst-case inhalation exposure of 44 mg/m^3 is proposed for these activities.

- 40 mg/m^3 for silk screening
- 44 mg/m^3 for general printing.

Dermal exposure

Measurements

In a study performed in Finland by the Kuopio Regional Institute of Occupational Health (Riskofderm, 2003b), a part of the EU Riskofderm project, potential hands exposure to an other glycol ether EGBE (2-butoxyethanol, vapour pressure 0.1 kPa at 20°C) was measured during silk screening on 10 workers in three different enterprises. The measurements were made for 6 to 8

hours by giving protective gloves, which were collected after shift and analysed. Results (given in formulation) are presented in table 4.20. In the same study, measurements of actual hand exposure indicate that the use of gloves does lower hand exposure significantly. Hands seemed to the most dominant potential dermal route exposure because EGBE could be found only on a few parts of the body parts of printers.

Table 4.20: Potential dermal exposure measurements during silk screening (KRIOH, 2003)

	1st measurement day (µg/cm²/h)	2nd measurement day (µg/cm²/h)
No of samples	6	10
Average	5.328[a]	4.068[b]
90th %	15.684	12.937

a : 3 results were below the limit of detection
b : one result was below the limit of detection
The range of measured exposure values for formulation was <0.04-85 mg and the 90th percentile was 65 mg (unpublished data).

Modelling

Dermal exposure may occur during mixing, application and cleaning activities. Intermittent contact seems appropriate for this scenario (as for painting). Assuming non dispersive use, direct handling and intermittent contact, the EASE model estimates a dermal exposure in the range of 0.1-1 mg of product/cm²/day. The estimation is made for a formulation containing up to 35 % (silk screen inks) or 20 % (others) of PGMA and an exposed skin surface area of 840 cm² (two hands). This leads to an estimated external dermal exposure of:

- 29-294 mg/day for silk screening
- 17-168 mg/day for general printing.

Assessment

For general printing, no relevant exposure data are available. The EASE estimate therefore has to be used for risk characterisation. For silk screen printing, a set of 16 potential full shift hand exposure data is available with a 90th percentile of 65 mg of product. The "product" in this case consisted of a printing ink with up to 10% of EGBE and a retarder (up to 100% EGBE) that was used by just two of the printers (as part of the total ink-system). Assuming that the concentration of PGMA in screen printing inks can be up to 35 %, the reasonable worst case exposure level for PGMA in this process would be approximately 23 mg/day. Because the measured values are based on more than 12 measurements and come from different workplaces, they can be considered sufficiently representative for use in risk characterisation.

In conclusion, the following range are proposed for dermal exposure during printing:

- 23 mg/day for silk screening
- 168 mg/day for general printing.

Dermal exposure may be much lower if suitable gloves are worn.

- **Miscellaneous**

In 2000 and 2001, a study was performed in France to estimate the levels of exposure to glycol ethers in a sample population of 109 men employed by the Paris municipality by measuring the amount of alkoxycarboxylic acid metabolites in their urine (Ben-Brik E. *et al*., 2004). All men worked in maintenance, cleaning, transport, data processing and communication departments of the municipality, 54 were judged to be occupationally exposed to glycol ether-containing products. 2-MPA (2-methoxy propionic acid) was the most frequently found metabolite and it was also the metabolite that presented the highest concentrations reaching 5.6 mmol/mol creatinine. The mean concentration was 1.12 mmol/mol creatinine (range: 0.29-4.52) after the first day and 1.22 mmol/mol creatinine (range: 0.28-5.58) after the 2nd day. The authors conclude that particular attention should be paid in the future to alkoxypropionic acids derived from minor isomers of propylene glycol ether derivatives.

4.1.1.2.4 Summary of occupational exposure

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).

Table 4.21: Summary of proposed reasonable worst case exposures

Scenario	8-hour TWA inhalation (mg/m^3)	External dermal exposure (mg/day)
1 - Manufacture	3.5	42
2 - Formulation	43	2,000 (loading) 1,000 (filling)
3 - Use of products 3.1 Coating/Painting* - Industrial Spraying Other works - decorative 3.2 Printing - silk screening - general printing	 71 71 71 40 44	 3,000 360 120 23 168

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

4.1.1.3 Consumer exposure

4.1.1.3.1 Exposure from uses

PGMA is used in some consumer products. The identified consumer products are aqueous paints, floor varnishes and cleaning agents..

In Europe, PGMA is used as tension agent in aqueous paints and in floor varnishes at concentration ranging to 20% (FIPEC 2004). The concentration of PGMA used in cleaning products is at maximum 20%.

With respect to the above mentioned indicated consumer uses of PGMA and the availability of information especially about the concentration of PGMA in the consumers products two exposure scenario are considered: aqueous paints and floor varnishes and house cleaners..

Scenario 1: Aqueous paints and floor varnishes

When PGMA is used as an ingredient in aqueous paints and floor varnishes, the main exposure routes are by inhalation and by skin contact. The concentration of PGMA in paints and floor varnishes is at maximum 20%. No measured data was found about dermal and inhalation exposure of consumers by paints during their use or after their application.

Also as worst case, we will take as values of consumers exposure that retained for the exposure of the workers in the scenario of painting by brush and roller application.

The external exposure will be **71 mg/m^3**

Assuming a respiratory volume a day of 20 m^3 and a bodyweight of 60 kg, the external inhalation exposure is:

71 x 20/60 = **23.7 mg/kg/d**

For dermal exposure, the EASE model estimates a dermal exposure in the range of 0.1-1 mg of product/cm^2/day (non dispersive use with direct handling and intermittent contact). The estimation is made from a formulation containing up to 20% of PGMA and an exposed skin surface area of two hands of 840 cm^2.
This lead to estimated external dermal exposure of: 16.8-168 mg/day

Assuming a bodyweight of 60 kg, the external dermal exposure is: **0.3–2.8 mg/kg/d**.

Scenario 2: House cleaners

When PGMA is used as an ingredient in house cleaners the main exposure routes are by skin contact and by inhalation. The concentration of PGMA in house cleaners is at maximum 20%. No data was found about dermal exposure and inhalation exposure of consumers using house cleaners during their use.

The consumer exposure to PGMA is estimated with model of Technical Guidance Document.

Inhalation exposure

In the Technical Guidance Document, data from AISE (2002) are provided for use of surface cleaners : the highest quantity of liquid surface cleaner used is 110 g/task when it is diluted in 5 L of wash water volume and the longest duration of exposure is 20 minutes.

Assuming 20% of PGMA in house cleaners, 30% of house cleaners evaporate and a room volume of 20 m^3, the concentration in air is :

$$C_{inh} = \frac{110 \times 10^3 \times 0.2 \times 0.3}{20} = \mathbf{330\ mg/m^3}$$

For inhalation, based on a 20 m^3 respiratory volume a day for an adult weighing 60 kg and a 20 minutes (1/3 hour) duration of exposure, the exposure will be:

$$I_{inh} = \frac{330 \times 20 \times 1}{60 \times 24 \times 3} = \mathbf{1.5\ mg/kg/j}$$

Skin exposure

For dermal exposure, assuming direct handling and intermittent contact, the EASE model estimates a dermal exposure in the range of 1-5 mg of product/cm^2/day for wide dispersive use. Assuming 70% of house cleaners non evaporate, surface area of two hands of 840 cm^2 and 20% of PGME in house cleaners, estimated external dermal exposure is: 117.6-588 mg/day

Assuming a bodyweight of 60 kg, the external dermal exposure is: **2–9.8 mg/kg/d**

4.1.1.3.2 Summary of consumer exposure

Table 4.22: Summary of proposed reasonable worst case exposures in the main scenarios

SCENARIO	INHALATION (MG/M³)	INHALATION (MG/KG/D)	SKIN (MG/KG/D)	SUM OF EXPOSURES (MG/KG/D)
1. AQUEOUS PAINTS AND FLOOR VARNISHES	71	23.7	2.8	26.5
2. HOUSE CLEANERS	330	1.5	9.8	11.3

4.1.1.4 Humans exposed via the environment

The information relating to the estimation of the indirect exposure of humans via the environment are presented in table 4.23. The concentrations calculated in intake media (drinking water, fish, plant roots and leaves, milk, meat, air) and the subsequent estimation of human intakes via different routes are shown hereafter with the corresponding total daily intakes. Both local and regional levels are taken into consideration and the estimation of local environmental exposures has been performed for all scenarios listed in chapter 2.2. 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 for the body weight for which a value of 60 kg as been used. Absorption by dermal, oral and inhalation routes is taken as it has been defined for the consumers, i.e. 10%, 100% and 100% respectively.

Table 4.23: concentrations for indirect exposure of humans via the environment and subsequent total daily intakes

	Conc. in drinking water (mg.L^{-1}) / Subsequent daily dose (mg.kg^{-1}.d^{-1})	Conc. in wet fish (mg.kg^{-1}) / Subsequent daily dose (mg.kg^{-1}.d^{-1})	Conc. in plant roots (mg.kg^{-1}) / Subsequent daily dose (mg.kg^{-1}.d^{-1})	Conc. in plant leaves (mg.kg^{-1}) / Subsequent daily dose (mg.kg^{-1}.d^{-1})	Conc. in milk (mg.kg^{-1} ww) / Subsequent daily dose (mg.kg^{-1}.d^{-1})	Conc. in meat (mg.kg^{-1} ww) / Subsequent daily dose (mg.kg^{-1}.d^{-1})	Conc. in air (mg.m^{-3}) / Subsequent daily dose (mg.kg^{-1}.d^{-1})	Total daily intake (mg.kg^{-1}.d^{-1})
Production (site-specific, worst case)	0.0871 / 2.90×10^{-3}	0.0833 / 1.60×10^{-4}	0.0837 / 5.35×10^{-4}	0.331 / 6.62×10^{-3}	1.58×10^{-3} / 2.56×10^{-6}	2.74×10^{-5} / 1.37×10^{-7}	0.0597 / 0.0199	0.0301
Paints and coating:								
- Water based: Formulation	0.153 / 5.10×10^{-3}	0.216 / 4.14×10^{-4}	0.0423 / 2.71×10^{-4}	0.0202 / 4.03×10^{-4}	8.11×10^{-5} / 7.59×10^{-7}	8.11×10^{-6} / 4.07×10^{-8}	3.6×10^{-3} / 1.20×10^{-3}	7.39×10^{-3}
Processing	0.0933 / 3.11×10^{-3}	0.132 / 2.53×10^{-4}	0.0376 / 2.41×10^{-4}	0.182 / 3.63×10^{-3}	1.7×10^{-4} / 1.59×10^{-6}	1.7×10^{-5} / 8.53×10^{-8}	0.0327 / 0.0109	0.0182
Private use	1.69×10^{-3} / 5.62×10^{-5}	1.99×10^{-3} / 3.82×10^{-6}	1.62×10^{-3} / 1.04×10^{-5}	1.39×10^{-3} / 2.77×10^{-5}	1.73×10^{-6} / 1.61×10^{-8}	1.73×10^{-7} / 8.66×10^{-10}	2.49×10^{-4} / 8.30×10^{-5}	1.81×10^{-4}
- Solvent based: Formulation	0.229 / 7.63×10^{-3}	0.323 / 6.20×10^{-4}	0.0733 / 4.69×10^{-4}	0.187 / 3.75×10^{-3}	2.33×10^{-4} / 2.18×10^{-6}	2.33×10^{-5} / 1.17×10^{-7}	0.0338 / 0.0113	0.0237
Processing	0.197 / 6.55×10^{-3}	0.266 / 5.10×10^{-4}	0.189 / 1.21×10^{-3}	2.06 / 0.0413	1.56×10^{-3} / 1.45×10^{-5}	1.56×10^{-4} / 7.81×10^{-7}	0.372 / 0.124	0.174
Private use	1.69×10^{-3} / 5.62×10^{-5}	1.99×10^{-3} / 3.82×10^{-6}	1.62×10^{-3} / 1.04×10^{-5}	1.39×10^{-3} / 2.77×10^{-5}	1.73×10^{-6} / 1.61×10^{-8}	1.73×10^{-7} / 8.66×10^{-10}	2.49×10^{-4} / 8.30×10^{-5}	1.81×10^{-4}
Electronic industry: Processing	0.0192 / 6.39×10^{-4}	0.0178 / 3.40×10^{-5}	0.0184 / 1.18×10^{-4}	2.01×10^{-3} / 4.02×10^{-5}	9.78×10^{-6} / 9.15×10^{-8}	9.78×10^{-7} / 4.91×10^{-9}	3.48×10^{-4} / 1.16×10^{-4}	9.47×10^{-4}
Chemical industry: chemicals used in synthesis: Processing	0.0722 / 2.41×10^{-3}	0.062 / 1.19×10^{-4}	0.0693 / 4.43×10^{-4}	1.75×10^{-3} / 3.5×10^{-5}	3.27×10^{-5} / 3.05×10^{-7}	3.27×10^{-6} / 1.64×10^{-8}	2.58×10^{-4} / 8.61×10^{-5}	3.09×10^{-3}
Printing inks: Formulation	0.0537 / 1.79×10^{-3}	0.0758 / 1.45×10^{-4}	0.0157 / 1.00×10^{-4}	7.86×10^{-3} / 1.57×10^{-4}	2.9×10^{-5} / 2.71×10^{-7}	2.9×10^{-6} / 1.46×10^{-8}	1.4×10^{-3} / 4.68×10^{-4}	2.66×10^{-3}
Processing	5.77×10^{-3} / 1.92×10^{-4}	2.89×10^{-3} / 5.54×10^{-6}	5.54×10^{-3} / 3.55×10^{-5}	0.0107 / 2.14×10^{-4}	1.02×10^{-5} / 9.49×10^{-8}	1.02×10^{-6} / 5.09×10^{-9}	1.93×10^{-3} / 6.43×10^{-4}	1.09×10^{-3}
Metal cleaning: Formulation	0.0363 / 1.21×10^{-3}	0.0512 / 9.82×10^{-5}	0.011 / 7.02×10^{-5}	5.7×10^{-3} / 1.14×10^{-4}	1.99×10^{-5} / 1.86×10^{-7}	1.99×10^{-6} / 9.89×10^{-9}	1.02×10^{-3} / 3.40×10^{-4}	1.83×10^{-3}
Processing	4.16×10^{-3} / 1.39×10^{-4}	4.14×10^{-3} / 7.94×10^{-6}	3.99×10^{-3} / 2.56×10^{-5}	1.4×10^{-3} / 2.80×10^{-5}	2.81×10^{-6} / 2.63×10^{-8}	2.81×10^{-7} / 1.41×10^{-9}	2.49×10^{-4} / 8.30×10^{-5}	2.83×10^{-4}
Detergents, cleaners: Formulation	0.0145 / 4.83×10^{-4}	0.0205 / 3.92×10^{-5}	5.13×10^{-3} / 3.28×10^{-5}	3×10^{-3} / 6.01×10^{-5}	8.46×10^{-6} / 7.91×10^{-8}	8.46×10^{-7} / 4.24×10^{-9}	5.38×10^{-4} / 1.79×10^{-4}	7.94×10^{-4}
Processing	2.61×10^{-3} / 8.71×10^{-5}	2.8×10^{-3} / 5.36×10^{-6}	2.51×10^{-3} / 1.61×10^{-5}	1.39×10^{-3} / 2.78×10^{-5}	2.13×10^{-6} / 1.99×10^{-8}	2.13×10^{-7} / 1.07×10^{-9}	2.49×10^{-4} / 8.30×10^{-5}	2.19×10^{-4}
Adhesive: Private Use	1.8×10^{-3} / 6.01×10^{-5}	2.55×10^{-3} / 4.88×10^{-6}	1.7×10^{-3} / 1.09×10^{-5}	1.39×10^{-3} / 2.78×10^{-5}	1.78×10^{-6} / 1.66×10^{-8}	1.78×10^{-7} / 8.91×10^{-10}	2.49×10^{-4} / 8.30×10^{-5}	1.87×10^{-4}

	Conc. in drinking water (mg.L^{-1}) / Subsequent daily dose (mg.kg^{-1}.d^{-1})	Conc. in wet fish (mg.kg^{-1}) / Subsequent daily dose (mg.kg^{-1}.d^{-1})	Conc. in plant roots (mg.kg^{-1}) / Subsequent daily dose (mg.kg^{-1}.d^{-1})	Conc. in plant leaves (mg.kg^{-1}) / Subsequent daily dose (mg.kg^{-1}.d^{-1})	Conc. in milk (mg.kg^{-1} ww) / Subsequent daily dose (mg.kg^{-1}.d^{-1})	Conc. in meat (mg.kg^{-1} ww) / Subsequent daily dose (mg.kg^{-1}.d^{-1})	Conc. in air (mg.m^{-3}) / Subsequent daily dose (mg.kg^{-1}.d^{-1})	Total daily intake (mg.kg^{-1}.d^{-1})
Regional	1.41×10^{-3} / 4.70×10^{-5}	1.99×10^{-3} / 3.82×10^{-6}	8.52×10^{-4} / 5.45×10^{-6}	1.38×10^{-3} / 2.77×10^{-5}	1.6×10^{-6} / 1.50×10^{-8}	1.6×10^{-7} / 8.04×10^{-10}	2.49×10^{-4} / 8.30×10^{-5}	1.67×10^{-4}

The highest indirect exposure is estimated for the processing of solvent-borne paints and coating: 0.174 $mg.kg^{-1}.day^{-1}$. It can also be noted that the highest exposures are to be expected through intake of air and leaves of plants. Moreover, based on the regional concentrations, the total daily intake for humans is 1.67×10^{-4} $mg.kg^{-1}.day^{-1}$. These two figures will be taken forward into the risk characterisation.

4.1.2 Effects assessment: Hazard identification and dose (concentration)-response (effect) assessment

This part of the report is based extensively on the OECD SIDS dossier dated 2 October 2000 (rapporteur: Japan). The reporting of the studies and the conclusions are the same as those reached by OECD. Only a few details have been added in this report and some studies which were not included in the SIDS dossier. For this reasons, some studies in this report are not reported in details, but have been approved at OECD level.

4.1.2.1 Toxicokinetics, metabolism and distribution

Several studies confirmed that rapid and extensive hydrolysis of PGMA to PGME (Propylene Glycol Methyl Ehter) occurred *in vivo* when PGMA was administered by oral, inhalatory (Miller *et al.,* 1984) or dermal route (Sumner, 1999). Since urinary metabolites and disposition profiles of PGMA were approximately identical to the results obtained with PGME (Miller *et al.* 1984), it is unlikely that there are substantial differences of the systemic toxicity between PGMA and PGME. In fact, toxicity of PGMA is almost the same of PGME.

4.1.2.1.1 Studies in animals

Inhalation

A single 6 h-inhalation (3000 ppm (16.5 mg/l)) study in male rats was conducted using [1-^{14}C] labeled PGMA (Miller *et al.,* 1984). About 53 % and 26 % of the radioactivities (aquired body burden) were eliminated via lungs as $^{14}CO_2$ and via urine within 48 hours, respectively. Complete recovery of the radioactivity occurred within 48 hr indicating no accumulation in the body (see table below). Tissue distribution was from the higher to the lower concentration: liver, blood, fat, kidneys. The urinary metabolites consisted of propylene glycol, propylene glycol monomethyl ether (PGME), and its sulfate and glucuronide conjugates, indicating rapid and extensive hydrolysis of PGMA to PGME *in vivo.*

Table 4.24: Percentages of total radioactivity recovered after exposure to 3000 ppm PGMA

Organs	%
Urine	26.0 ± 1
Feces	2.7 ± 0.8
Charcoal	5.4 ± 0.5
CO_2	52.6 ± 3.1
Carcass	7.5 ± 0.5
Skin	3.1 ± 0.3
Cage wash	2.7 ± 0.2

Dermal

In recent experiment, the blood pharmacokinetics of PGMA and PGME in male rats was conducted following a single 6-hr dermal exposure at 100 or 1,000 (nominal) mg/kg (Sumner, 1999). Dermal application of PGMA at 130 mg/kg and 935 mg/kg resulted in the average PGME AUC (Area Under the Curve) of 88 and 1,580 ug/mL, respectively. Similarly, PGME application gave the average PGME AUC of 288and 15,051 ug/mL at the dose of 126 and 995 mg/kg, respectively. When AUCs were normalised to applied dose in terms of mmole basis, the mean combined PGME AUC after PGMA and PGME application were 0.0044 AUC/dose and 0.0141 AUC/dose, respectively. When AUC/dose of PGME is compared to that of PGMA, the ratio is 0.315, meaning that the efficiency of dermal absorption for PGMA is approximately 30% of that of PGME in rats. This work demonstrates that the existing extensive toxicological database for PGME is relevant for PGMA hazard assessment purposes (Sumner, 1999).

Oral

A single oral dose (8.7 mmol/kg) and 6 h-inhalation studies in male rats were conducted using ^{14}C labeled PGMA (Miller *et al.,* 1984). In oral study, about 64 % and 24 % of the radioactivities were eliminated via lungs as $^{14}CO_2$ and via urine within 48 hours, respectively. Complete recovery of the radioactivity occurred within 48 hr indicating no accumulation in the body (see table below). Tissue distribution was from the higher to the lower concentration: liver, blood, fat, kidneys. Unchanged PGMA was not present in urine and the urinary metabolites consisted of propylene glycol, propylene glycol monomethyl ether (PGME), and its sulfate and glucuronide conjugates, indicating rapid and extensive hydrolysis of PGMA to PGME *in vivo*.

Table 4.25: Percentages of total radioactivity recovered after exposure to 8.7 mmol/kg po dose of PGMA

Organs	%
Urine	23.8 ± 0.6
Feces	1.8 ± 0.6
Charcoal	2.1 ± 0.3
CO_2	63.5 ± 0.4
Carcass	6.0 ± 0.7
Skin	1.9 ± 0.9
Cage wash	0.9 ± 0.2

Other routes

Kinetic properties of PGMA were assessed in rats after IV administration of 14.7 or 147 mg/kg doses (Dow chemical company, 2001). Blood samples were taken 5, 10, 15, 30, 45 minutes and 1, 2, 4, 6, 8 and 12 hours after dosing for determination of PGME and PGMA. Half live of blood PGMA was 1.55 and 3.37 minutes for the low and high dose respectively and the plasma time course of PGMA was identical to PGME for equivalent dose.

In vitro studies

Rat blood and liver homogenates were incubated with PGMA concentrations of 5 and 50 µg/ml (Dow chemical company, 2001). Samples were analysed for PGME and PGMA contents at 1, 2, 4, 6, 8, 10, 15, 20, 30, 45 minutes and 1, 2, 4 and hours after the beginning of the study. This study was concurrently preformed with human blood and liver homogenates. The hydrolysis half life was lesser in rat blood than in human blood: about 15 minutes in rats and 35 min in human. For liver homogenates, similar half lives were found in human and in rat: values between 27 and 34 minutes.

4.1.2.1.2 Studies in humans

In vitro studies

Human blood and liver homogenates were incubated with PGMA concentrations of 5 and 50 µg/ml (Dow chemical company, 2001). Samples were analysed for PGME and PGMA contents at 1, 2, 4, 6, 8, 10, 15, 20, 30, 45 minutes and 1, 2, 4 and hours after the beginning of the study. This study was concurrently preformed with rat blood and liver homogenates. PGMA half live in blood was greater in human than in rat whereas similar values were found for liver homogenate half lives (see § *in vitro* animal studies for more details).

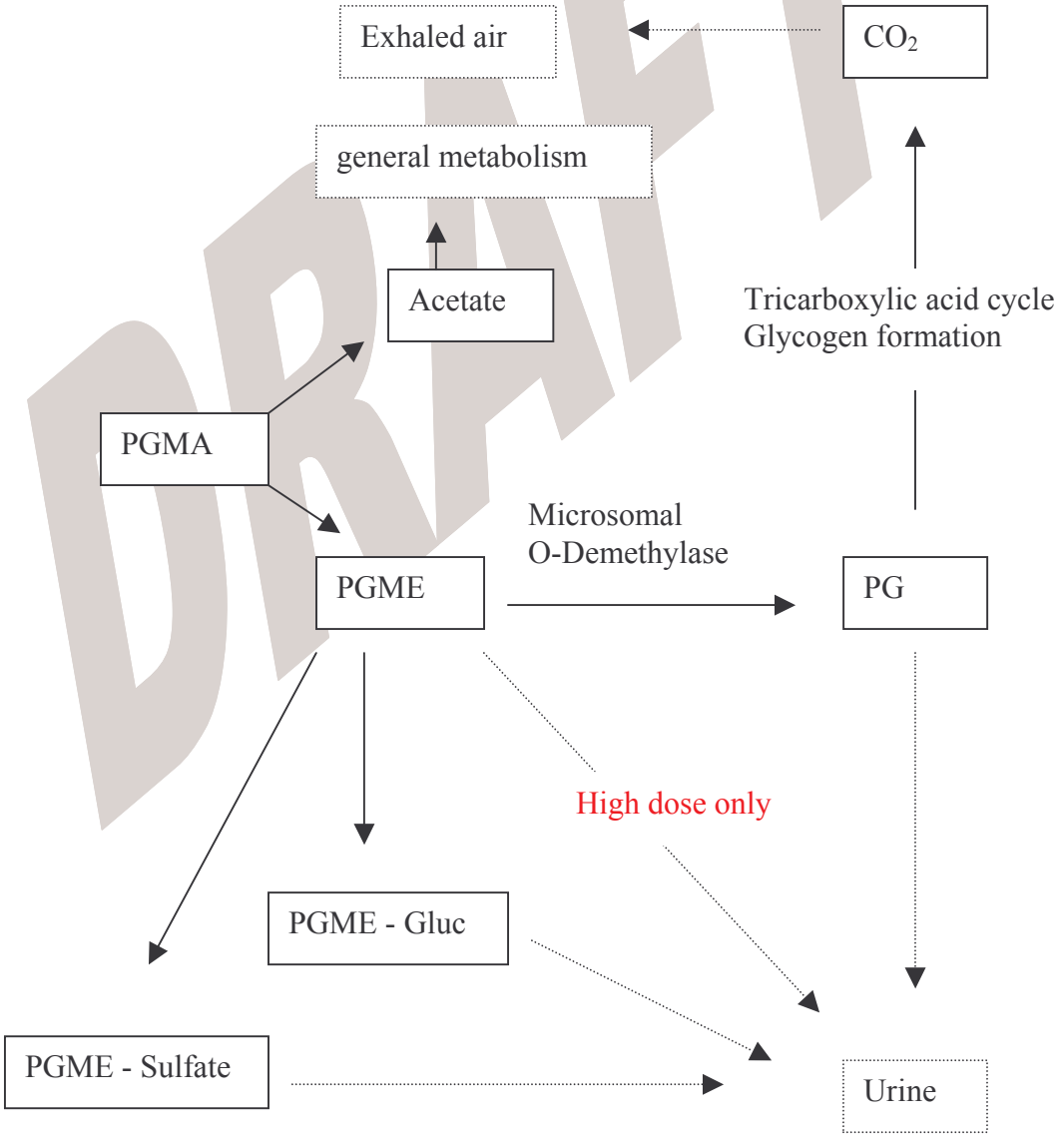
4.1.2.1.3 Summary of toxicokinetics, metabolism and distribution

PGMA is readily absorbed via oral and inhalation route. An absortion percentage of 100 % can be taken into account for these routes of exposure. Dermal absorption of PGMA is lesser than PGME (between 3 and 4 fold less). For dermal absorption it was found that dermal absorption for PGMA was approximately 30% of that of PGME in rats: an absorption factor of 10 % will hence be taken into account for RC.

PGMA is rapidly hydrolysed *in vivo* in PGME and acetate (blood half life of PGMA is about 2 min for a low dose of PGMA). Hydrolysis can also occur locally (i.e. in the respiratory tract). A detailed assessment of the PGME metabolism is available in the PGME RAR (see r406_0508_hh).

PGMA has the same metabolic pathway as PGME :

Figure 4.26: Metabolic pathway of PGMA



The maximum concentrations of PGMA are found in liver and blood. There is no signs of accumulation after exposure.

Elimination occur by urine as metabolites and by pulmonary elimination of CO_2 formed by the metabolism of PG (about 50 % of PGMA doses by this way of elimination).

4.1.2.2 Acute toxicity

4.1.2.2.1 Studies in animals

Inhalation

Rat

Rat were exposed 8 hours at concentrated vapour of PGMA (unknown purity) (Union Carbide Corporation, 1961).
No mortality was obtained (0/6).

Exposure of rats to a saturated atmosphere of PGMA (purity unknown) at a nominal concentration of 4,345 ppm (23,463 mg/m³) during 7 hours caused no adverse effects. (Dow Chemical Company, 1980).

In a GLP study, Fischer 344 rats were exposed head only at a PGMA (purity unknown) concentrations of 0 – 300 (1,620 mg/m³) and 2,000 ppm (10,800 mg/m³) during 3 hours (Dow Chemical Company, 1985).

Respiratory frequency was reduced in rats exposed to 2,000 ppm (10,800 mg/m³). Mortality data was not reported.

Mouse

In a GLP study, B6C3F1 mice were exposed head only at a PGMA (purity unknown) concentrations of 0 – 300 (1,620 mg/m³) and 2,000 ppm (10,800 mg/m³) during 3 hours (Dow Chemical Company, 1985).
Respiratory frequency was reduced in mice exposed to 2,000 ppm (10,800 mg/m³). Mortality data was not reported.

Dermal

Rat

Rat were exposed dermally to PGMA (purity unknown) at dose of 5,000 mg/kg (Dow Chemical Company, 1980).
Lethargy was noted after application of the 5,000 mg/kg dose. No dose-related lesion were observed upon gross pathology.

Fischer 344 rats were exposed dermally to undiluted PGMA (purity unknown) during 24 hours according a method described by Noakes and Sanderson (1969). Following a range finding study, 10 animals (5 males and 5 females) were doses with 2000 mg/kg (SHELL, 1985b). Animals were observed for clinical signs for 14 days after dosing. Body weights were recorded the first day, day 7 and day 14 after dosing. No systemic effects were observed

during the observation period, the only effect observed was an inflammation of the site of administration which generally completed in 7 days.

Rabbit

Rabbit were administered PGMA (purity unknown) dermally at dose of 20 ml/kg bw (19,432 mg/kg bw) (Union Carbide Corporation, 1961).

No mortality was reported (0/4).

Oral

Acute toxicity of PGMA (unknown purity) was tested in rats (Union Carbide Corporation, 1961). LD50 was found to be > 14.1mL(13,700mg)/kg b.w.(male).
Deaths, preceded by a narcotic-like state, occurred from one to three days after dosing. Gross examination at autopsy revealed congested lungs, kidneys and adrenals; mottled congested livers with prominent acini; and gastrointestinal haemorrhage. In one rat, bladder contained bloody urine.
Fischer 344 rats (5/sex/group) were dosed orally with PGMA (purity unknown) at doses ranging from 1,564 to 10,000 mg/kg bw (Shell, 1985b). Animals were observed for clinical signs for 14 days after dosing. Body weights were recorded the first day, day 7 and day 14 after dosing. Clinical signs included gait abnormalities, increased lacrimation and/or salivation and coma. LD50, calculated in males and females were 6190 mg/kg bw and 5155 mg/kg bw respectively.

Male and female Fischer 344 rats were administered orally at doses of 500, 1,000, 2,000, 4,000, 6,300, and 10,000mg/kg bw and observed for two weeks (Dow Chemical Company, 1992). Signs of toxicity were lethargy, piloerection, watery eyes, anorexia, shallow breathing and/or excess salivation. Mortality was recorded only for female rats at 10,000mg/kg bw. Gross pathology revealed no treatment-related changes at the end of two weeks for both sexes. From these results, acute toxicity of PGMA is considered to be low.

4.1.2.2.2 Studies in humans

No data available for PGMA. However some human studies are available in human for PGME and are reported here.

Male human subjects were exposed to increasing concentrations of PGME from 50 to 1000 ppm (187 to 3740 mg/m^3) (2050 ppm (7700 mg/m^3) in one case) (Steward *et al*., 1970). Duration of exposure was up to 7 hr at concentrations up to 250 ppm (935 mg/m^3) and up to 2 hr at concentrations up to 2050 ppm. See the following table for experimental conditions:

Table 4.27: Experimental condition for human exposure in the Steward study

		Vapor concentration, ppm			
Experiment	No of subjects	Mean	SE	Range	Duration of exposure, hr
1	1	47.3	0.2	44.8-50.0	1
2	6	95	0.5	89.0-101.0	3.5
3	1	240.9	0.1	236.0-243.0	1
4	6	231.4	0.8	223.0-250.0	1.25
5	5	242.6	1.0	229.0-269.0	1.25
6	6	249	2.9	200.0-297.0	3.5
7	5	239	1.1	221.0-266.0	7
8	2	1056	4.3	0-2050.0	2

The substance become noticeable at 10 ppm (37 mg/m^3). Above 100 ppm (374 mg/m^3), the odor was transiently objectionable; eyes were slightly irritated after 1-2 hr exposure. At 300 ppm (1122 mg/m^3), there was mild eye and nasal irritation within 5 minutes which became intolerable after 1 hr. 750 ppm (2800 mg/m^3) was scored as very strongly irritating. At 1000 ppm, indications of CNS depression were recognized. Breath analysis data demonstrated that PGME was rapidly excreted via the lungs. The human volunteers all experienced rapid development of odor tolerance. Hence, unless prompt action is taken when objectionable odor is experienced, it cannot be relied upon to prevent exposures that may be hazardous. However, because the odor is readily detected and is objectionable, PGME vapours are considered to have adequate warning properties, if needed. Neurologic, clinical, chemical and general medical studies did not show any significant abnormalities. In this study, the NOAEC for CNS depression was 750 ppm. This value will be taken into account in the risk characterisation.

4.1.2.2.3 Summary of acute toxicity

Acute toxicity of this chemical is low in rodents because LD50 values are greater than 5,000 mg/kg bw by oral or dermal routes and greater than 10,800 mg/m^3 by inhalation, moreover a nominal concentration of 23,463 mg/m^3 did not cause adverse effects.

No classification is needed whichever the route of exposure.

Table 4.28: summary of acute toxicity studies

Experimental condition	LD/LC 50	Effects	Validity	Reference
Inhalation route				
Inhalation Rat		Concentrated vapour (8h) LC_0	2	Union Carbide Corporation, 1961
Inhalation Rat (6h)		LC_0 23,463mg/m^3	2	Dow Chemical Company, 1980
Inhalation Rat (3h)		LC_0 10,800mg/m^3 (male)	2	Dow Chemical Company, 1985
Inhalation Mouse (3h)		LC_0 10,800mg/m^3 (male)	2	Dow Chemical Company , 1985
Dermal route				
Dermal Rat	> 5,000 mg/kg		2	Dow Chemical Company., 1980
Dermal Rat	> 2000 mg/kg	Inflammation on the site of administration, no systemic effects	2	SHELL, 1985b
Dermal Rabbit		LC_0 19,400mg/kg	2	Union Carbide Corporation, 1961
Oral route				
Oral Rat	13,700mg/kg bw (male)		2	Union Carbide Corporation, 1961
Oral Rat	6190 mg/kg bw (male) 5155 mg/kg bw (female)	Gait abnormalities, coma/	2	SHELL, 1985b
Oral Rat	>10,000mg/kg bw (male) 8,532mg/kg bw (female)		2	Dow Chemical Company, 1992

4.1.2.3 Irritation

4.1.2.3.1 Skin

In two distinct studies, application of PGMA induced no skin irritation in rabbits (Dow Chemical Company, 1980 - Union Carbide Corporation, 1961).

Rabbits (3 males and 3 females) were tested in a semi-occlusive patch test to assess skin irritation produced by PGMA (purity unknown) (SHELLl, 1985b). PGMA was applied during 4 hours, observation were made 30 min, 24, 48, 72 hours and 7 days after removal of the patch. No signs of irritation were seen in this study.

Summary skin irritation:

PGMA was found to be not irritant in 3 studies performed on rabbits. No classification is needed for this end-point.

4.1.2.3.2 Eye

In an eye irritation study on rabbits (Union Carbide Corporation, 1961), eye injury of Grade 2 was noted. This result led to a classification as irritant for the eye. No more detail are available concerning this study.

Eye irritancy of PGMA (purity unknown) was determined by using draize method (SHELL, 1985b). Six rabbits were tested and eyes were not washed after application. A visual assessment of the eye irritancy was made at 1, 24, 48, 72 hours and 7 days after application. Irritancy was scored for the cornea, iris and conjunctivae using the standard Draize scores. Severe initial pain was observed for each rabbit. The group mean 24, 48 and 72 hour scores were 1.1 for redness, 0.2 for chemosis and 0 for corneal opacity and iris effects. In this study, PGMA can be considered as a mild irritant and results does not warrant any classification for eye irritancy.

PGMA (purity unknown) caused, moderate conjunctival redness, slight conjunctival swelling, slight discharge, slight iritis and corneal opacity when applied to the eye of female New Zealand white rabbits (not washed) (Dow Chemical Company, 1980). Mean scores for 9 rabbits were, for corneal opacity 0.2, for iris lesions 0.1, for conjunctival redness 0.8 and for chemosis 0.5. All signs of irritation had disappeared after 4 days. According to the results of this study, the substance do not need to be classify as an eye irritant according to the EEC criteria (Dow, 1993).

Summary eye irritation

In an old study, PGMA was found to be a mild to severe eye irritant, with initial pain at instillation. In well performed recent studies, irritation scores found were below the limits of classification for eye irritancy. Therefore, no classification is needed for eye irritation.

4.1.2.3.3 Respiratory tract

No data available.

Hydrolysis of PGMA to PGME and acetate in the respiratory tract could lead to mild signs of irritation. (see Miller *et al.* 1984 in RDT section)

With PGME slight signs of irritation were observed in one study (Steward *et al*., 1970). At 250 ppm, three subjects had throat irritation and one had nose irritation after 15-30 minutes exposure, and 15 subjects complained of nose irritation and 2 of throat irritation after 45-60 minutes. At 500 ppm nose and throat irritation were severe after 30 minutes of exposure and at 700 ppm, rhinorrhea was observed. At 2000 ppm, the subject was unwilling to breathe

through his nose because of the pain caused by the vapour and he complained of a very severe sore throat. The NOAEC for local effects on the respiratory tract was 100 ppm for PGME.

In other study, measurement of pre- and post-exposure eye redness, corneal thickness, tear film break-up time, conjuctival epithelial damage, blinking frequency, and subjective ratings were used to evaluate the possible irritating effects of PGME (Emmen *et al.*, 2003). There were no objective eye irritation effects at doses of 100 and 150 ppm. Subjective effects were reported at 150 ppm.

4.1.2.3.4 Summary of irritation

In animal studies (rabbits), PGMA was found to be non-irritating to the skin and mildly irritating to the eye. PGMA is not expected to be severely irritant for the respiratory tract at usual PGMA levels of exposure. No classification is needed for irritation.

For risk characterisation, a cross-reading can be done with PGME and the NOAEC of 100 ppm will be taken into account for local effects on the respiratory tract.

4.1.2.4 Corrosivity

PGMA is not a corrosive substance

4.1.2.5 Sensitisation

4.1.2.5.1 Studies in animals

Skin

Hartley Guinea pig were tested for PGMA sensitising properties in a modified test (see Maguire H.C., 1973) (Dow Chemical Company, 1980). Application of PGMA induced no skin sensitisation.

In a GLP Magnusson-Kligman maximisation test, Hartley-Dunkin guinea pigs were treated with PGMA (Dow Chemical Company, 1985b). No signs of sensitisation were recorded.

In a Magnusson-Kligman maximisation test, guinea pigs were treated with PGMA (purity unknown) (SHELL, 1985b). None of the 20 test animals showed any positive response at either 24 or 48 hours after removal of the challenge patches.

In a Magnusson-Kligman maximisation test, Hartley-Dunkin guinea pigs were treated with PGMA (purity > 99%) (Zissu, 1995). No signs of sensitisation were recorded.

In four sensitisation tests, PGMA did not induce sensitisation in treated guinea pigs.

Respiratory tract

No data. But due to SAR with other glycol ethers, PGMA is not expected to be a respiratory tract sensitiser.

4.1.2.5.2 Studies in humans

No data

4.1.2.5.3 Summary of sensitisation

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

4.1.2.6 Repeated dose toxicity

4.1.2.6.1 Studies in animals

Inhalation

Rat

Short-term vapour inhalation toxicity was studied for F344 rats for males and females at a dose of 0, 300, 1,000 or 3,000 ppm (0, 1.62, 5.39 or 16.18 mg/L) for six hours per day on 5 consecutive days, followed by 4 additional consecutive days of exposure after a weekend interruption (Miller *et al.,* 1984). Purity was 95.2 % (4.6 % of other isomer acetate)

After two weeks experimental period, haematology and clinical chemistry analyses revealed no treatment-related changes. However, the kidneys of all male rats and two of five females in the 3,000 ppm-exposure group appeared to be slightly reticulated at necropsy. Other slight renal changes were also observed histologically in one of five male rats at 1,000 ppm. The change noted in these animals was a slight increase in the eosinophilic granularity of the proximal convoluted tubules of the kidneys. This renal change observed at 1,000 and 3,000 ppm seems to be uncertain whether it is solely due to the accumulation of the male rat specific protein complex, alpha-2mglobulin, because female rats in addition to male rats suffered from kidney lesion at 3,000 ppm, equivalent to an approximate dose of 2,000 mg/kg/day. Another histologically detectable effect in rats was slight-to-moderate degeneration of olfactory epithelium in the nasal cavities of three of five males and one of five females in the 3,000 ppm-exposure group. This nasal change is likely caused by acetic acid from PGMA hydrolysis at the exposure site. A NOAEC was established at 300 ppm (1.62 mg/L) for males and at 1,000 ppm (5.39 mg/L) for females.

In a GLP study, male Fischer 344 were exposed 4 days whole body to PGMA (purity unknown) by inhalation, 6 h/day for 4 days ; 3 h/day on 5th day at doses of 0, 300 ppm (1,620 mg/ m3), 2,000 ppm (10,800 mg/m3) (Dow Chemical Company, 1985c).
In one out of the four animals tested in the 2000 ppm group (10,800 mg/m3), a slight degree of degeneration and flattening of the olfactory epithelium was detected in one side of the nasal cavity. This change occurred near the most anterior excursion of the olfactory epithelium in the dosal meatus and was characterised by loss of cells in the neuron layer and flattening of the sustentacular cell layer, resulting in decreased thickness of the neuroepithelium at the affected sites. In this study a NOAEC of 300 ppm (1,620 mg/m3) was identified based on effects seen at 2,000 ppm (10,800 mg/m3).

Mouse
Short-term vapour inhalation toxicity was studied for B6C3F1 mice for males and females at a dose of 0, 300, 1,000 or 3,000 ppm (0, 1.62, 5.39 or 16.18 mg/L) for six hours per day on 5 consecutive days, followed by 4 additional consecutive days of exposure after a weekend interruption (Miller *et al.,* 1984). Purity was 95.2 % (4.6 % of other isomer acetate)

After two weeks experimental period, haematology and clinical chemistry analyses revealed no treatment-related changes. The only histopathologic changes occurred in the nasal cavities. Degeneration of olfactory epithelium, similar to that observed in rats, was present to some degree in all male and female mice in the 300, 1,000 and 3,000 ppm exposure group. This acute degenerative change occurred in a dose-related manner, although this change was minimum at 300 ppm, and was generally more severe and more extensive in animals exposed to 3,000 ppm (16.18 mg/L). A NOAEC was not established and LOAEC was 300 ppm (1.62 mg/L) for males and females. According to these results, mice were more sensitive than rats to developing olfactory epithelium degeneration following inhalation exposure.

B6C3F1 male Mice were exposed buy inhalation to PGMA (purity unknown) 6 h/day for 4 days at concentrations of 0, 300 ppm (1,620 mg/m3), 2,000 ppm (10,800 mg/m3) (Dow Chemical Company, 1985c)
Respiratory frequency decreased in mice at 2,000 ppm (10,800 mg/m3). All mice exposed to 300 ppm (1,620 mg/m3) or 2,000 ppm (10,800 mg/m3) had degeneration of olfactory epithelium. Very slight (3 of 4 mice) to slight (1 of 4 mice) olfactory degeneration at 300 ppm (1,620 mg/m3) and slight (4 of 4 mice) olfactory degeneration at 2,000 ppm (10,800 mg/m3). In this study a LOAEC of 300 ppm (1,620 mg/m3) is identified.

Dermal

No data.

Oral

Using an OECD combined repeat dose and reproductive/developmental toxicity screening test [OECD TG 422], SD (Crj: CD) rats were received gavage doses of 0 (vehicle; distilled water), 100, 300 and 1,000 mg/kg bw/day, for males for 44 days from 2 weeks prior to mating and for females for 41-45 days from 14 days before mating to day 3 postpartum (Ministry of Health & Welfare (Japan), 1998). Purity of 99.9%.
A dose of 1,000 mg/kg bw/day of PGMA exerted some effects in only male rats. Blood examination revealed decreases in glucose and inorganic phosphorus and an increase in relative weight of the adrenals was noted in males. However, such changes were not observed in females. Histopathological examination revealed none of the alteration of tissues at the highest dose group for both sexes. As such changes in males were considered not to be adverse effect, a NOAEL was considered to be 1,000 mg/kg bw/day for both sexes.

4.1.2.6.2 Studies in humans

No data.

4.1.2.6.3 Summary of repeated dose toxicity

The NOAEL for repeat dose oral toxicity (by gavage) in rats was 1,000 mg/kg bw/day for both sexes. An inhalation study reveals that the critical effects are toxicity in kidney and nasal cavities in rats, whereas only degeneration of olfactory epithelium occurs in mice. A NOAEC for repeat inhalation systemic toxicity in rats was established at 300 ppm (1.62 mg/L) for males and at 1,000 ppm (5.39 mg/L) for females. However, a NOAEC for inhalation toxicity in mice (local effects) was not established because the lowest dose at 300 ppm (1.62 mg/L) induced a minimum effect on nasal cavity. For local effects (degeneration of olfactory epithelium) a LOAEC of 300 ppm can be taken into account.

Regarding general systemic toxicity, only short term studies are available (2 weeks), and in these studies only renal effects specific to male rat were observed. As PGMA is rapidly hydrolysed *in vivo* to PGME, the results obtained for PGME can apply for chronic toxicity. In this case, a NOAEL of 300 ppm could be taken into account for systemic effects based on the 2-year rat study performed with PGME and leading to liver effects at doses of 1000 ppm.

In absence of dermal data for PGMA, dermal data on PGME will be used for dermal risk characterisation: no systemic effects were reported at 1000 mg/kg (the only tested dose in a 21-day study by dermal route).

4.1.2.7 Mutagenicity

4.1.2.7.1 Studies *in vitro*

In a GLP Bacterial reverse mutation assay, Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, TA1538 were treated with PGMA (purity unknown), with and without metabolic activation, at doses of 50, 10, 1.0, 0.1 mg/plate (Dow Chemical Company, 1983). For metabolic activation mammalian metabolic preparations were used. (pre-incubation assay).

PGMA was not genotoxic in this study.

PGMA was tested for reverse gene mutation in Salmonelle typhimurium strains TA1535, TA1538, TA98, TA 100 and Escherichia coli WP_2 uvrA with and without metabolic activation at doses up to 4000 µg/plate (SHELL, 1985). In the same study, PGMA was also tested for mitotic gene conversion in Saccharomyces cerevisiae JD1 with and without metabolic activation at doses up to 5 mg/ml. No cytotoxicity was observed. PGMA did not induced reverse gene mutation in the bacterial tests and did not produced mitotic gene conversion in Saccharomyces.

In a GLP Bacterial reverse mutation assay (OECD Guidelines No.471 and 472) on Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, Escherichia coli WP2 uvr A, PGMA (purity: >99.9 %) was administered at concentrations of 0, 0.313, 0.625, 1.25, 2.50, 5.00 mg/plate (without S 9) and 0, 0.313, 0.625, 1.25, 2.50, 5.00 mg/plate (with S 9) (Ministry of Health & Welfare (Japan), 1998). For metabolic activation, mammalian metabolic preparations were used (pre-incubation assay) Cytotoxicity was not observed up to 5.00mg/plate (five strains) with and without metabolic activation. No genotoxic effects were seen in this study.

PGMA was tested for genotoxicity on CHO cells at doses up to 3000 µg/ml in the presence of metabolic activation and up to 7500 µg/ml without metabolic activation (SHELL, 1985). In the presence of metabolic activation, 3000 µg/ml PGMA reduced the percentage of cells at metaphase to 63 % of that seen in control culture whereas in the absence of metabolic activation, concentration up to 7500 µg/ml did not produced any effect. There was no significant, dose-related increase in the frequency of chromatide gaps or total chromatide aberrations. A relatively high number of chromatide gaps were observed at the higher dose in the absence of metabolic activation (7500 µg/ml) but were not considered as a positive response by the authors because: gaps were considered as incidental achromatic regions and no other types of chromosome damage were observed in cultures exposed to PGMA with or without metabolic activation.

GLP Chromosomal aberration test by OECD TG 473 was conducted in cultured Chinese hamster lung (CHL/IU) cells. Concentrations of PGMA (puirity > 99.9 %) tested were: 0, 0.33, 0.65, 1.30 mg/mL with and without metabolic activation. Structural chromosomal aberrations and polyploidy were not induced up to a maximum concentration of 1.3 mg/mL (10 mM) on continuous treatment, and with short-term treatment, with and without an exogenous metabolic activation system (Ministry of Health & Welfare (Japan), 1998).

Using rat primary cell cultures of hepatocytes, PGMA failed to elicit significant unscheduled DNA synthesis (method OECD 482) at any of the concentrations tested (0.1, 0.0316, 0.01, 0.00316, 0.001, 0.000316, 0.0001, 0.0000316 M), while PGMA was toxic to the hepatocyte cultures at 0.0316 and 0.1M as indicated by detachment of cells and/or a granular appearance (Mandrala A.L., 1983 - Dow Chemical Company, 1983).

4.1.2.7.2 Studies *in vivo*

No data

4.1.2.7.3 Summary of mutagenicity

This chemical is not genotoxic with and without an exogenous metabolic activation system in bacterial test and chromosomal aberration test *in vitro*. PGMA did not induce UDS in rat hepatocytes.

4.1.2.8 Carcinogenicity

No data

4.1.2.8.1 Summary of carcinogenicity

PGMA id rapidly hydrolysed to PGME. There is a 2-year study available on PGME which has showed that no carcinogenicity is expected. This can also apply for PGMA (for thr PGME moiety).

The main concern could be du to the formation of acetate and the effects on the nasal epithelium. The degenerative effects seen in the 3-week study may lead to carcinogenic effect due to local irritation and subsequent enhanced cell proliferation. This would be due to the

acetate moiety only. This hypothetical effect will not be taken into account in the risk characterisation for carcinogenicity because:

- in general no ester acetate is classified for carcinogenicity by inhalation route,
- this irritant effect will be taken into account in the repeated dose toxicity section

4.1.2.9 Toxicity for reproduction

4.1.2.9.1 Effects on fertility

Using OECD combined repeat dose and reproductive/developmental toxicity screening test [OECD TG 422], SD (Crj: CD), rats received gavage PGMA (purity > 99.9 %) doses of 0 (vehicle; distilled water), 100, 300 and 1,000 mg/kg/day, for males for 44 days from 2 weeks prior to mating and for females for 41-45 days from 14 days before mating to day 3 postpartum. The animals were sacrificed on the day 4 of lactation for females (MHW, Japan: 1998). No effects related to chemical exposure were observed maternally at 1,000 mg/kg, although there was a single unsuccessful copulation at this dose level which was not statistically significantly different from the control ($p<0.05$). Similarly, no effects related to the chemical exposure were observed in foetal data at 1,000 mg/kg. Reproductive toxicity of PGMA in rats by oral administration is not observed at the highest dose. A NOAEL was thus established at 1,000 mg/kg bw/day.

The NOAEL derived from the screening test is consistent with the NOAEL derived from the PGME studies (1000 mg/kg bw). Due to the rapid hydrolysis of PGMA to PGME *in vivo*, the results obtained with PGME can be used for PGMA.

4.1.2.9.2 Developmental toxicity

In a GLP study, pregnant SD female rats were exposed to PGMA (purity: 97.3% of 2-methoxy-1-methylethyl acetate and 2.0 % of 1- methoxy-2-) methylethyl acetate) vapour from Days 6 through 15 of gestation, once daily for 6 hours/day at nominal dose of 0, 500, 2,000, 4,000 ppm (0, 2,700, 10,800, 21,600 mg/m3). The animals were sacrificed on Day 20 of gestation to evaluate the potential maternal, embryonic and teratogenic parameters of PGMA (USAEHA, 1989). Most of the effects observed in dams were transient in nature. Reductions in muscle tone (2,000 and 4,000 ppm), food consumption (500, 2,000 and 4,000 ppm) and body weight (2,000 and 4,000) were seen during the exposure period. At 2,000 and 4,000 ppm exposure groups, dyspnea, ruffled pelt and red discharges from the eyes or mouth were observed. No toxic signs were observed in the 500 ppm exposure group. The effect on nasal cavity was not examined in this experiment. No developmental toxicity was observed. A NOAEC was established at 500 ppm (2,700 mg/m3, measured) for dams and 4,000 ppm (22,464 mg/m3, measured) for foetuses.

4.1.2.9.3 Summary of toxicity for reproduction

PGMA did not produce any fertility effects in rats A NOAEL of 1000 mg/kg were seen in a screening study via oral route. In this study, effects on oestus cycle were not recorded. Due to the metabolism of PGMA, effects seen with PGME can be expected (see 2 generation study

by inhalation route with PGME). These effects led to a NOAEC of 1000 ppm (5400 mg/m^3 for PGMA). This NOAEC can be taken into account for PGMA.

For developmental effects, there was no evidence of teratogenicity of PGMA in an inhalation study performed on rats. In this study a NOAEL of 500 ppm (2,700 mg/m3) was observed for dams for systemic toxicity and 4,000 ppm (22,464 mg/m3) for foetuses for developmental effects (no effects at the highest tested dose).

4.1.3 Risk characterisation [5]

4.1.3.1 General aspects

The human population may be exposed to PGMA at the workplace, both from use of consumer products and indirectly via the environment (see 4.1.1.1, 4.1.1.2 and 4.1.1.3).

The main routes of potential exposure to PGMA are via inhalation and across the skin as identified under 4.1.1.1, Exposure assessment: general discussion.

For dermal absorption it was found that dermal absorption for PGMA was approximately 30% of that of PGME in rats. An absorption factor of 10 % will hence be taken into account for risk characterization.

From the oral absorption studies it is concluded that oral absorption is complete. For risk characterisation 100 % oral absorption should be assumed. No quantitative data is available of absorption by inhalation route, but all studies showed that PGMA is readily absorbed via inhalation route, an absorption percentage of 100 % will be taken into account. For dermal absorption it was found that dermal absorption for PGMA was approximately 30% of that of PGME in rats. Based on the 10 % of dermal absorption for PGME (see PGME RAR), whole body exposure to vapour PGMA gives hence a contribution of about 3.3 % maximum of the total body burden due to dermal absorption. For liquid PGMA, an absorption percentage of 10 % can be taken into account (based on the dermal absorption rate estimate of 30 % for PGME, see PGME RAR).

For interspecies extrapolation, PBPK models exist for the rat, mouse and human. These enable some kinetic extrapolations. The model available, Corley *et al*.,2005 is considered complete and appropriate for potential use in the derivation of an interspecies extrapolation factor for all routes of exposure because it has been experimentally validated and covers relevant routes of exposure. Moreover this model has also been accepted for another glycol ether: EGBE.

According to this model a interspecies factor of 0.4 can be taken into account for extrapolation of values found in rats to values estimated in humans for exposure concentrations above 100 ppm and of 1 for exposure concentrations below 100 ppm since according to Corley *et al.*, 2005 the rat and human blood levels of PGME are similar at exposure concentrations below 100 ppm.

[5] Conclusion (i) There is a need for further information and/or testing.
Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Acute toxicity of this chemical is low in rodents because LD_{50} values are greater than 5,000 mg/kg by oral or dermal routes and greater than 10,800 mg/m^3 by inhalation.

This chemical is mildly irritating to eye, but not to skin. PGMA is not skin-sensitising in guinea pigs. For irritation, it is proposed to do a cross-reading with PGME data and to use the NOAEC of 100 ppm derived from a human study.

For repeated dose toxicity, inhalation studies demonstrated that PGMA caused local irritation effect at doses of 300 ppm and higher (probably because of the hydrolysis *in situ* in PGME and acetate). A LOAEC for local effects was found to be 300 ppm. For systemic effects, studies available are only short term studies and therefore do not allow a good assessment of chronic properties of PGMA. In this case, a cross-reading with PGME is possible due to the rapid hydrolysis of PGMA to PGME *in vivo*. A NOAEC derived from the 2-year rat PGME study will be taken into account for chronic effects of PGMA: 300 ppm (based on liver effects observed at higher doses, 1000 ppm and higher). As no data exists on PGMA via dermal route, the NOAEL of PGME will be taken into account (1000 mg/kg/day) (see PGME RAR).

Two bacterial mutation tests, unscheduled DNA synthesis in rat hepatocytes and chromosomal aberration test *in vitro* show negative results. An UDS study was also negative.

No data is available for carcinogenicity. Cross-reading with PGME data is possible because of the rapid hydrolysis of PGMA to PGME and acetate. No carcinogenic properties are expected for PGME moiety and risk of seeing carcinogenic development due to the local irritation caused by the acetate moiety is taken into account by the RDT risk characterisation.

PGMA did not produce any fertility effects in rats. A NOAEL was established at 1,000 mg/kg bw/day by gavage (the highest tested dose). Cross reading with PGME data would lead to a fertility NOAEC of 1000 ppm by inhalation (effects in females). For developmental effects, there was no evidence of teratogenicity of PGMA in an inhalation study performed on rats. In this study a NOAEL of 500 ppm (2,700 mg/m3) was observed for dams for systemic toxicity and 4,000 ppm (22,464 mg/m3) for foetuses for developmental effects (no effects at the highest tested dose).

Table 4.28bis: Summary of effects

Substance name	Inhalation (N(L)OAEC)	Dermal (N(L)OAEL)	Oral (N(L)OAEL)
Acute toxicity	> 10,800mg/m^3 750 ppm* or 2800 mg/m^3 – CNS depression in human PGME data (4116 mg/m^3)	> 5000 mg/kg	> 5000 mg/kg
Irritation / corrositivity	< 300 ppm (100 ppm from PGME data)	NA	NA
Sensitization	NA	NA	NA
Repeated dose toxicity (local)	< 300 ppm	ND	NA
Repeated dose toxicity (systemic)	300 ppm *(1620 mg/m^3)	> 1470 mg/kg *	NA
Mutagenicity	NA	NA	NA
Carcinogenicity	ND	ND	ND
Fertility impairment	1000 ppm **	NA	NA
Developmental toxicity	NA	NA	NA

NA: not applicable

ND: no data

- * based on PGME data (conversion factor of 1.47 (conversion of PGME dermal dose to PGMA dermal dose)
- ** based on PGME data and is consistent with the results of the screening study.

4.1.3.2 Workers

Table 4.29: Summary of proposed reasonable worst case exposures

Scenario	8-hour TWA inhalation (mg/m^3)	Dermal (to be updated) (mg/day)
1 - Manufacture	3.5	42
2 - Formulation	43	3000 (loading and filling)
3 - Use of products 3.1 Coating/Painting* - Industrial		
Spraying	71	3000
Other works	71	360
- decorative	71	120
3.2 Printing	40	23
silk screening	44	168
general printing		

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

4.1.3.2.1 Acute toxicity

Given the toxicity observed in the dermal studies and the anticipated occupational exposure levels it is concluded that PGMA is of no concern for workers with regards to acute dermal effects. (**Conclusion ii**).

By inhalation, the CL50 is greater than 10,800 mg/m^3 by inhalation with PGMA. However, CNS depression was observed in humans exposed to PGME. A NOAEC of 750 ppm, which corresponds to 4116 mg/m3 of PGMA, has been derived from human exposure and taken into account for acute inhalation CNS risk characterisation. This NOAEC is compared with levels of exposure. The MOSs obtained are compared with minimal MOS calculated as follows:

Table 4.29bis Assessment factors applied for the calculation of minimal MOS for acute toxicity (for inhalation route).

Interspecies differences	1
Intraspecies differences	5 (workers: homogen population)
Type of effect	1
Confidence of the database	1
Minimal MOS	5

Table 4.29ter : MOS and conclusions of the risk assessment for acute inhalation toxicity of PGMA.

Scenario	8-hour TWA inhalation (mg/m^3)	MOS	Conclusion
1 - Manufacture	3.5	1176	ii
2 - Formulation	43	96	ii
3 - Use of products			
3.1 Coating/Painting*			
- Industrial			
Spraying	71	58	ii
Other works	71	58	ii
- decorative	71	58	ii
3.2 Printing			
silk screening	40	103	ii
general printing	44	94	ii

Conclusion ii is reached for all occupational scenarios.

4.1.3.2.2 Irritation and corrosivity

Skin and eye irritation (liquid)

Given the effects observed in the skin and eye irritation studies it is concluded that PGMA is of no concern for workers with regard to irritating effects (**conclusion ii**).

Eye and upper respiratory tract irritation (vapours)

A NOEC of 100 ppm (549 mg/m^3) is taken for this effect (this value comes from a PGME study in volunteers). Since this NOEC is derived from humans, the only assessment factor needed is that to allow for possible intra-species variation. This is particularly true since the effects are not only discomfort in nature. A factor of 3, and therefore a minimal MOS of 3 is

considered sufficient for this end point. The MOSs between the NOEC and the inhalation exposure levels and the conclusions of the risk assessment are reported in table 4.29quater:

Table 4.29quater : MOS and conclusions of the risk assessment for eye and upper respiratory tract irritation with vapour exposure of PGMA.

Scenario	8-hour TWA inhalation (mg/m^3)	MOS	Conclusion
1 - Manufacture	3.5	157	ii
2 – Formulation (loading)	43	12.7	ii
2 – Formulation (filling)	43	12.7	ii
3 - Use of products 3.1 Coating/Painting*			
- Industrial (Spraying)	71	7.7	ii
- Industrial (Other works)	71	7.7	ii
- Decorative	71	7.7	ii
3.2 Printing			
- silk screening	40	13.7	ii
- general printing	44	12.4	ii

For eye and respiratory tract irritation due to the exposure of PGMA in vapour form, **conclusion ii** is reached for all scenarios.

4.1.3.2.3 Sensitisation

Given the effects observed in the dermal sensitisation studies it is concluded that PGMA is of no concern for workers with regard to skin sensitisation (**conclusion ii**).

There are neither data from human experience nor other indications for respiratory sensitisation (**conclusion ii)**.

4.1.3.2.4 Repeated dose toxicity

Systemic toxicity:

No pertinent data is available for PGMA (only short-term data are available). Due to the rapid hydrolysis of PGMA to PGME *in vivo,* a read-across to PGME has been adopted. A good chronic study exists for PGME. Given the kinetic properties of PGMA, it is possible to take this study into account for risk characterisation of PGMA

Liver effects were seen in this study leading to a NOAEC of 300 ppm (1620 mg/m^3).

This NOAEC is compared with levels of exposure. The MOSs obtained are compared with minimal MOS calculated as follows:

Table 4.30: Assessment factors applied for the calculation of minimal MOS for repeated dose toxicity (for inhalation and dermal route) (see PGME RAR).

Interspecies differences	2.5 (toxicodynamic factor) x 1[1] = 2.5 Dermal route: 2.5 x 2.4 = 6[2]
Intraspecies differences	5 (workers: homogen population)
Duration of exposure	2 [3]
Type of effect	1
Confidence of the database	1
Minimal MOS	12.5 for inhalation route 60 for dermal route

[1] the initial factor of 0.4 derived from Corley *et al.,* 2005 (difference in PGMA hydrolysis kinetic between rats and humans) was reassessed (see discussion in 4.1.3.1) and estimated at 1 at the concentration below 100ppm leading to a final interspecies factor of 2.5.

2 for dermal route, as a rabbit study is used as starting point, allometric scaling factor of 2.4 is applied, as recommended by the TGD.

3 a lower assessment factor of 2 was used instead of a factor of 6 as recommended by the TGD to extrapolate from 21-day to chronic study. This factor was reduced since no assessment factor was judged necessary to extrapolate from sub-acute to sub-chronic study since the NOAEL retained from 21-day study was lower than the NOAEL found in an old dermal 90-day study.

Inhalation

NOAEC of 1,620 mg/m^3 is compared with exposure estimates. The results are summarised in table 4.31.

Based on the risk assessment for inhalation exposure, it is concluded that toxicity due to repeated exposure is not expected for all scenarios (**conclusion ii**).

Conclusion ii is reached for all other occupational scenarios

Dermal:

No data on PGMA. Dermal NOAEL, from PGME studies, is greater or equal to 1000 mg/kg/day for repeated toxicity (systemic, 21-day study). This value is supported by the NOAEL of the 90-day study (Rowe *et al.*, 1954) where a NOAEL of 2 ml/kg bw (1838 mg/kg bw of PGME) was identified. This NOAEL of 1470 mg/kg (for PGMA) is compared to exposure estimates. The results are summarised in table 4.31.

Based on the risk assessment for dermal exposure, it is concluded that toxicity due to repeated exposure are not expected for all scenario except for the formulation and industrial spraying scenarios. Conclusion (iii) are drawn for these two scenarios.

Conclusion ii is reached for the other occupational scenarios: manufacture, coating/painting (industrial other works and decorative) and for printing (silk screening and general printing).

Table 4.31: Occupational risk assessment of PGMA for repeated dose toxicity.

Scenario		Risk assessment for inhalation exposure			Risk assessment for dermal exposure to liquid PGMA		
		8-hour TWA inhalation (mg/m^3)	MOS	Conclusion	Estimated Skin exposure mg/day worst case (mg/kg bw/d	MOS	Conclusion
1 - Manufacture		3.5	463	ii	42 (0.6)	2450	ii
2 – Formulation		43	37	ii	3000 (42.9)	34	iii
3 - Use of products	3.1 Coating/Painting						
	Industrial - spraying	71	23	ii	3000 (42.9)	34	iii
	Industrial - other works	71	23	ii	360 (5.1)	288	ii
	Decorative	71	23	ii	120 (1.7)	865	ii
	3.2 Printing						
	Silk screening	40	40	ii	23 (0.33)	4455	ii
	General printing	44	37	ii	168 (2.4)	613	ii

Combined exposure:

For the combined exposure, the estimated internal doses are calculated from the biological exposure data. Inhalation exposure will give internal dose of:

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) = Y (inhalation internal dose).

So, the NOAEC of 1620 mg/m³ would lead to an internal doses of 231 mg/kg.

This internal dose should be compared with internal dose calculated. This NOAEC should be compared with internal doses calculated from exposures in each scenario (inhalation + dermal). The internal doses are calculated as follow:

This value does not take into account the possible dermal absorption of vapour during the 8hr TWA. It has been demonstrated that dermal absorption of vapour PGMA could count for 3.3 % of the internal dose of PGMA. To take into account this value, the value of internal dose due to dermal exposure to vapours (Z) should by added to the former value (Y). Z represent 3.3 % of the total internal dose and can be calculated as follow :

Z = 0.03/0.97 x Y = 0.03 Y

The total internal dose due to inhalation exposure (inhalation output + dermal vapour penetration output) is Y + Z = 1.03 Y

In this case, an internal dose of about 6.93 mg/kg (0.03 Y) can be calculated, to obtain a total internal dose of 237.9 mg/kg due to inhalation and dermal absorption of PGMA.

For dermal exposure internal dose is calculated for a 70 kg bw worker with a percentage of absorption of 10 % (extrapolation from PGME).

The minMOS is the same as for inhalation exposure. Internal doses corresponding to each scenarios, MOS and conclusions are summarised in table 4.32:

Table 4.32: Risk characterisation for combined exposure – repeated dose toxicity

Scenario		Risk assessment for combined exposure				
		Internal dose after inhalation exposure Y + Z (mg/kg)	Internal dose after dermal exposure to liquid PGMA (mg/kg) 10 %	Total internal dose (inhalation + dermal combined exposure)	MOS	Conclusion
1 - Manufacture		0.5	0.06	0.56	425	ii
2 – Formulation		6.3	4.3	10.6	22.4	ii
3 - Use of products	3.1 Coating/Painting					
	Industrial					
	- spraying	10.4	4.3	14.7	16.2	ii
	- other works	10.4	0.51	10.91	21.8	ii
	Decorative	10.4	0.17	10.57	22.5	ii
	3.2 Printing					
	Silk screening	5.9	0.03	5.93	40.1	ii
	General printing	6.5	0.24	6.74	35.3	ii

Assuming a worker of 70 kg, a respiratory volume of 10 m^3/workday, an inhalation absorption of 100 % and a dermal absorption of 10 %.

Based on the risk assessment for combined exposure, it is concluded that toxicity due to repeated exposure are not expected (**Conclusion ii**).

Local effects:

For local effects a LOAEC of 300 ppm (1620 mg/m^3) was found in RDT studies conducted with PGMA (irritation of the respiratory tract probably due to *in situ* hydrolysis in PGME and acetate). A risk characterisation is needed or this end-point but only for inhalation exposure.

This LOAEC is compared with levels of exposure. The MOSs obtained are compared with minimal MOS calculated as follows:

Table 4.33: Assessment factors applied for the calculation of minimal MOS for acute toxicity (for inhalation and dermal route).

Interspecies differences	2.5 (toxicodynamic factor) (toxicokinetic factor not applied for local effects)
Intraspecies differences	5
Extrapolation LOAEC to NOAEC	3
Type of effect	1
Confidence of the database	1
Minimal MOS	37.5 for inhalation route

Table 4.34: Risk characterisation for inhalation exposure – local effects

Scenario		Risk assessment for inhalation exposure – local effects		
		8-hour TWA inhalation (mg/m^3)	MOS	Conclusion
1 - Manufacture		3.5	463	ii
2 – Formulation		43	38	ii
3 – Use of products	3.1 Coating/Painting			
	Industrial (spraying and other works)	71	23	iii
	Decorative	71	23	iii
	3.2 Printing			
	Silk screening	40	40	ii
	General printing	44	37	ii

Based on the risk assessment for inhalation, dermal and combined exposure for repeated systemic toxicity, it is concluded that toxicity due to repeated exposure can be excluded for all scenario (**conclusion ii**).

Based on the risk assessment for local effects (chronic irritation of the respiratory tract) due to repeated exposure by inhalation, a risk is expected for coating and painting scenario: industrial (spraying and other works) and decorative. **Conclusion iii.** For the other scenarios, a conclusion (ii) is drawn.

4.1.3.2.5 Mutagenicity

Given the effects observed in the mutagenicity studies it is concluded that PGMA is of no concern for workers with regard to mutagenicity (**conclusion ii**).

4.1.3.2.6 Carcinogenicity

Given the effects observed in the carcinogenicity study of PGME it is concluded that PGMA is of no concern for workers with regard to carcinogenicity (**conclusion ii**).

4.1.3.2.7 Toxicity for reproduction

Effects on fertility

A NOAEL of 1000 mg/kg were seen in a screening study via oral route. In this study, effects on oestus cycle were not recorded. Due to the metabolism of PGMA, effects seen with PGME can be expected (see 2 generation study by inhalation route with PGME). These effects led to a NOAEC of 1000 ppm (5400 mg/m^3 for PGMA). This NOAEC can be taken into account for PGMA.

This NOAEC is compared with levels of exposure. The MOSs obtained are compared with minimal MOS calculated as follows:

Table 4.35: Assessment factors applied for the calculation of minimal MOS for reproductive toxicity (for inhalation and dermal route) (see PGME RAR).

Interspecies differences	2.5 (toxicodynamic factor) x 1[1] = 2.5 Dermal route: 4 x2.5=10
Intraspecies differences	5
Type of effect	1
Confidence of the database	1
Minimal MOS	12.5 for inhalation route 50 for dermal route

[1] the initial factor of 0.4 from Corley *et al.*, 2005 (difference in PGMA hydrolysis kinetic between rats and humans) was reassessed (see discussion in 4.1.3.1) and estimated at 1 at concentration below 100ppm leading to a final interspecies factor of 2.5.

Inhalation

NOAEC of 5400 mg/m^3 is compared with exposure estimates. The results are summarised in the following table 4.36.

Based on the risk assessment for inhalation exposure, it is concluded that toxicity to fertility is not expected for all occupational scenarios (**conclusion ii**)

Dermal:

No dermal NOAEL is available for fertility assessment. A NOAEL can be extrapolated from inhalation NOAEC using the following parameters:

For MOS calculation: the rat inhalatory NOAEC of 5,400 mg/m^3 has been converted into dermal NOAEL (in mg/kg bw/day) by using a 6 h respiratory volume of 0.29 m^3/kg bw (200 ml/min / 250g bw = 0.8 l/min/kg bw) for the rat and a correction for differences in absorption between rats and humans.

$$\text{corrected dermal N(L)OAEL} = \text{inhalatory N(L)OAEC} \times \text{sRV}_{\text{rat}} \times \frac{\text{ABS}_{\text{inh-rat}}}{\text{ABS}_{\text{derm-human}}}$$

sRV = standard respiratory volume

$\text{ABS}_{\text{inh – rat}}$ = 100%

$\text{ABS}_{\text{derm – Human}}$ = 10%

5,400 * 0.29 * 100 / 10 = 15,660 mg/kg bw/day

The dermal NOAEL is converted to internal dose taking into account 10% absorption via skin and compared to the systemic dose per day via skin for each scenario.

The results are summarised in table 4.36.

Based on the risk assessment for dermal exposure, it is concluded that reproductive toxicity (fertility) is not expected for all scenarios.

Table 4.36: Risk characterisation for inhalation and dermal routes – reproductive toxicity

Scenario		Risk assessment for inhalation exposure			Risk assessment for dermal exposure to liquid PGMA		
		8-hour TWA inhalation (mg/m^3)	MOS	Conclusion	Estimated Skin exposure mg/day worst case (mg/kg bw/d	MOS	Conclusion
1 - Manufacture		3.5	1542	ii	42 (0.6)	26100	ii
2 – Formulation		43	37	ii	3000 42.9	365	ii
3 - Use of products	3.1 Coating/Painting						
	Industrial - spraying	71	23	ii	3000 (42.9)	365	ii
	Industrial - other works	71	23	ii	360 (5.1)	3070	ii
	Decorative	71	23	ii	120 (1.7)	9211	ii
	3.2 Printing						
	Silk screening	40	40	ii	23 (0.33)	47454	ii
	General printing	44	37	ii	168 (2.4)	6525	ii

Combined exposure:

For the combined exposure, the estimated internal doses are calculated from the biological exposure data. Inhalation exposure will give internal dose of:

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 kg (mean bw of a worker) = Y (inhalation internal dose).

So, the NOAEC of 5400 mg/m³ would lead to an internal doses of 771 mg/kg.

This internal dose should be compared with internal dose calculated. This NOAEC should be compared with internal doses calculated from exposures in each scenario (inhalation + dermal). The internal doses are calculated as follow:

This value does not take into account the possible dermal absorption of vapour during the 8hr TWA. It has been demonstrated that dermal absorption of vapour PGMA could count for 3.3 % of the internal dose of PGMA. To take into account this value, the value of internal dose due to dermal exposure to vapours (Z) should by added to the former value (Y). Z represent 3.3 % of the total internal dose and can be calculated as follow :

$Z = 0.03/0.97 \times Y = 0.03\ Y$

The total internal dose due to inhalation exposure (inhalation output + dermal vapour penetration output) is $Y + Z = 1.03\ Y$

In this case, an internal dose of about 23.1 mg/kg (0.03 Y) can be calculated, to obtain a total internal dose of 794.1 mg/kg due to inhalation and dermal absorption of PGMA.

For dermal exposure, internal dose is calculated for a 70 kg bw worker with a percentage of absorption of 10 % (extrapolation from PGME).

The minimal MOS chosen for the combined exposure will be the one taken for inhalation exposure: 12.5 as it is the MOS calculated for the inhalation NOAEC which is taken into account in the calculations Internal doses corresponding to each scenarios, MOS and conclusions are summarised in table 4.37:

Table 4.37: Risk characterisation for combined exposure – reproductive toxicity

Scenario		Risk assessment for combined exposure				
		Internal dose after inhalation exposure Y + Z (mg/kg)	Internal dose after dermal exposure to liquid PGMA (mg/kg) 10 %	Total internal dose (inhalation + dermal combined exposure)	MOS	Conclusion
1 - Manufacture		0.5	0.06	0.56	1418	ii
2 – Formulation (loading)		6.1	4.3	10.4	76.3	ii
3 - Use of products	3.1 Coating/ Painting					
	Industrial					
	- spraying	10.4	4.3	14.7	54	ii
	- other works	10.4	0.51	10.91	72.8	ii
	Decorative	10.4	0.17	10.57	75.1	ii
	3.2 Printing					
	Silk screening	5.9	0.03	5.93	133.9	ii
	General printing	6.5	0.24	6.74	117.8	ii

Based on the risk assessment for combined exposure, it is concluded that toxicity to fertility due to combined exposure is not expected for all scenarios (**conclusion ii**).

Developmental toxicity

PGMA is not teratogenic. No effects were seen in foetuses without evident signs of maternal toxicity. It is concluded that that PGMA is of no concern for workers with regard to developmental toxicity (**conclusion ii).**

4.1.3.2.8 Summary of risk characterisation for workers

Conclusion ii is reached for all end points and all scenarios except for local effects (chronic irritation of the respiratory tract) due to repeated exposure for coating and painting scenario: industrial (spraying and other works) and decorative conclusion and for systemic toxicity due to repeated dermal exposure for formulation and industrial spraying scenarios (conclusion **iii)**.

4.1.3.3 Consumers

For risk characterisation, a value of 10 % for dermal absorption and a value of 100% for inhalation exposure can be taken into account.

Tableau 4.38: Internal dose exposure depending on scenarios

SCENARIO	INHALATION (MG/M³)	(MG/KG/D)	SKIN (MG/KG/D)	SUM OF EXPOSURES (MG/KG/D)
1. AQUEOUS PAINTS AND FLOOR VARNISHES	71.0	23.7	0.3	24.0
2. HOUSE CLEANERS	330	1.5	1.0	2.5

For repeated dose toxicity, and toxicity for reproduction, daily exposure level has to be averaged over a year. So the internal exposure dose used for risk characterisation is:

$$\frac{\text{internal dose} \times \text{number of events over a year}}{365}$$

Table 4.39: Internal dose exposure depending on scenarios average over a year

Scenario	Number of events	INHALATION (MG/KG/D)	SKIN (MG/KG/D) external	(MG/KG/D) internal	SUM OF EXPOSURES (MG/KG/D)
1. AQUEOUS PAINTS AND FLOOR VARNISHES	10 events/year	0.6	0.076	0.01	0.6
2. HOUSE CLEANERS	94-250/year*	1.0	6.7	0.7	1.7

* Data from the Technical Guidance Document

4.1.3.3.1 Acute toxicity

Given the toxicity observed in the acute dermal studies and the anticipated consumers exposure levels it is concluded that PGMA is of no concern for consumers with regards to acute dermal effects. (**Conclusion ii**).

By inhalation, the CL50 is greater than 10,800 mg/m³ by inhalation with PGMA. However, CNS depression was observed in humans exposed to PGME. A NOAEC of 750 ppm, which corresponds to 4116 mg/m3 of PGMA, has been derived from human exposure and taken into account for acute inhalation CNS risk characterisation. This NOAEC is compared with levels of exposure. The MOSs obtained are compared with minimal MOS calculated as follows:

Table 4.39bis Assessment factors applied for the calculation of minimal MOS for acute toxicity (for inhalation route).

Interspecies differences	1
Intraspecies differences	10
Type of effect	1
Confidence of the database	1
Minimal MOS	10

Table 4.39ter : MOS and conclusions of the risk assessment for acute inhalation toxicity of PGMA.

Scenario	Inhalation (mg/m^3)	MOS	Conclusion
1. Aqueous paints and Floor varnishes	71.0	58	ii
2. House cleaners	330	12.5	ii

Conclusion ii is reached for all consumer scenarios.

4.1.3.3.2 Irritation and corrosivity

Given the results from irritation and corrosivity studies, it is concluded that PGMA is of no concern for consumers with regard to irritation and corrosivity (**conclusion ii**)

Eye and respiratory tract irritation (vapours)

A NOEC of 100 ppm (549 mg/m^3) is taken for this effect (this value comes from a PGME study in volunteers). Since this NOEC is derived from humans, the only assessment factor needed is that to allow for possible intra-species variation. This is particularly true since the effects are not only discomfort in nature. A factor of 3, and therefore a minimal MOS of 3 is considered sufficient for this end point. The MOSs between the NOEC and the inhalation exposure levels and the conclusions of the risk assessment are reported in table 4.39quater.

Table 4.39quater: MOS and conclusion for eye and respiratory tract irritation

SCENARIO	Inhalation (mg/m^3)	MOS	Conclusion
1. AQUEOUS PAINTS AND FLOOR VARNISHES	71	7.7	ii
2. HOUSE CLEANERS	330	1.7	iii

For eye and respiratory tract irritation due to the exposure of PGMA in vapour form, **conclusion iii** is reached house cleaners scenario. **Conclusion ii** is reached for aqueous paints and floor varnishes.

4.1.3.3.3 Sensitisation

Given the results from sensitisation studies, it is concluded that PGMA is of no concern for consumers with regard to sensitisation (**conclusion ii**).

4.1.3.3.4 Repeated dose toxicity

Systemic toxicity

No pertinent data is available for PGMA. A good chronic study exists for PGME (6h/day and 5 days a week). Given the kinetic properties of PGMA, it is possible to take this study into account for risk characterisation of PGMA. Liver effects were seen in this study leading to a NOAEC of 300 ppm (1620 mg/m^3).

An internal dose corresponding to this NOAEC has to be calculated and compared with the internal daily exposures.

The daily inhalation volume for human is 20 m^3, the mean body weight is 60 kg and the absorption of PGMA by inhalation is 100%.

So the internal dose corresponding to the NOAEC of 1620 mg/m^3 is:

$$\frac{1620 \times 20}{60} \text{ x 6 x 5 /24 x 7 = 96 mg/kg/d}$$

The MOSs obtained are compared with minimal MOS calculated as follows:

Table 4.40: Assessment factors applied for the calculation of minimal MOS repeated dose toxicity (systemic effects).

Interspecies differences	Inhalation route: 2.5 (toxicodynamic factor) x 1[1] = 2.5* Dermal route: 2.5 x 2.4 = 6[2]
Intraspecies differences	10
Duration of exposure	2 [3]
Type of effect	1
Confidence of the database	1
Minimal MOS	25 for inhalation route 120 for dermal route

1 the initial factor of 0.4 derived from Corley *et al*., 2005 (difference in PGMA hydrolysis kinetic between rats and humans) was reassessed (see discussion in 4.1.3.1) and estimated at 1 at the concentration below 100ppm leading to a final interspecies factor of 2.5.
2 for dermal route, as a rabbit study is used as starting point, allometric scaling factor of 2.4 is applied, as recommended by the TGD.
3 a lower assessment factor of 2 was used instead of a factor of 6 as recommended by the TGD to extrapolate from 21-day to chronic study. This factor was reduced since no assessment factor was judged necessary to extrapolate from sub-acute to sub-chronic study since the NOAEL retained from 21-day study was lower than the NOAEL found in an old dermal 90-day study.

Inhalation

Result is summarised in table 4.41.

Dermal

No data on PGMA. Dermal NOAEL, from PGME studies, is greater or equal to 1,000 mg/kg/day for repeated toxicity (systemic, 21-day study). This value is supported by the NOAEL of the 90-day study (Rowe *et al.*, 1954) where a NOAEL of 2 ml/kg bw (1838 mg/kg bw of PGME) was identified. This NOAEL of 1470 mg/kg bw/d (for PGMA) is compared to external exposure. Result is summarised in table 4.41.

Sum of exposures

The internal dose of 96 mg/kg/d, corresponding to the NOAEC of 1620 mg/m^3, is compared with exposure estimate. Result is summarised in table 4.41:

Table 4.41: MOS and conclusion for repeated dose toxicity (systemic effects)

SCENARIO	Inhalation		Dermal		Sum of exposures	
	MOS	Conclusion	MOS	Conclusion	MOS	Conclusion
1. AQUEOUS PAINTS AND FLOOR VARNISHES	160	ii	19342	ii	160	ii
2. HOUSE CLEANERS	96	ii	219	ii	56	ii

Conclusion ii is reached for all consumers scenarios.

Local effects

For local effects a LOAEC of 300 ppm (1620 mg/m^3) was found in RDT studies (irritation of the respiratory tract probably due to *in situ* hydrolysis in PGME and acetate). A risk characterisation is needed for this end-point but only for inhalation exposure.

This LOAEC of 1620 mg/m^3 is compared with level of external exposure. The MOS obtained are compared with minimal MOS calculated as follows:

Table 4.42: Assessment factors applied for the calculation of minimal MOS repeated dose toxicity (local effects).

Interspecies differences	2.5 (toxicodynamic factor) (toxicokinetic factor not applied for local effects)
Intraspecies differences	10
Extrapolation LOAEC to NOAEC	3
Type of effect	1
Confidence of the database	1
Minimal MOS	75

The MOS between 1620 mg/m^{3}corresponding to the LOAEC and the inhalation exposure is reported in table 4.43:

Table 4.43: MOS and conclusion for repeated dose toxicity (local effects)

SCENARIO	Inhalation	
	MOS	Conclusion
1. AQUEOUS PAINTS AND FLOOR VARNISHES	23	iii
2. HOUSE CLEANERS	5	iii

Based on the risk assessment for inhalation exposure, it is concluded that local effects (chronic irritation of the respiratory tract) due to repeated exposure are expected for both scenarios. **Conclusion iii.**

4.1.3.3.5 Mutagenicity

Given the results from mutagenicity studies, it is concluded that PGMA is of no concern for consumers with regard to mutagenicity (conclusion ii).

4.1.3.3.6 Carcinogenicity

Given the results from carcinogenicity studies of PGME, it is concluded that PGMA is of no concern for consumers with regard to carcinogenicity (conclusion ii).

4.1.3.3.7 Toxicity for reproduction

Effects on fertility

A NOAEL of 1000 mg/kg were seen in a screening study via oral route. In this study, effects on oestus cycle were not recorded. Due to the metabolism of PGMA, effects seen with PGME can be expected (see 2 generation study by inhalation route with PGME; 6h/day and 5 days a week). These effects led to a NOAEC of 1000 ppm (5400 mg/m^3 for PGMA). This NOAEC can be taken into account for PGMA. An internal dose corresponding to this NOAEC has to be calculated and compared with the internal daily exposures.

The daily inhalation volume for human is 20 m^3, the mean body weight is 60 kg and the absorption of PGMA by inhalation is 100%. So the internal dose corresponding to the NOAEC of 5400 mg/m^3 is:

$$\frac{5400 \times 20}{60} \text{ x 6 x 5 /24 x 7 = 321 mg/kg/d}$$

The MOSs obtained are compared with minimal MOS calculated as follows:

Table 4.44: Assessment factors applied for the calculation of minimal MOS fertility effects.

Interspecies differences	Inhalation route: 2.5 (toxicodynamic factor) x 1[1] = 2.5 Dermal route: 10
Intraspecies differences	10
Type of effect	1
Confidence of the database	1
Minimal MOS	25 for inhalation route 100 for dermal route

1 the initial factor of 0.4 derived from Corley 2005 (difference in PGMA hydrolysis kinetic between rats and humans) was reassessed (see discussion in 4.1.3.1) and estimated at 1 at the concentration below 100ppm leading to a final interspecies factor of 2.5

Inhalation

The internal dose of 321 mg/kg/d, corresponding to the NOAEC of 5400 mg/m^3, is compared with exposure estimate. Result is summarised in table 4.45.

Dermal

No dermal NOAEL is available for fertility assessment. So, a NOAEL can be extrapolated from inhalation NOAEC using the following parameters:

For MOS calculation: the rat inhalatory NOAEC of 5,400 mg/m^3 has been converted into dermal NOAEL (in mg/kg bw/day) by using a 6 h respiratory volume of 0.29 m^3/kg bw (200 ml/min / 250g bw = 0.8 l/min/kg bw) for the rat and a correction for differences in absorption between rats and humans.

$$\text{corrected dermal N(L)OAEL} = \text{inhalatory N(L)OAEC} \times \text{sRV}_{\text{rat}} \times \frac{\text{ABS}_{\text{inh-rat}}}{\text{ABS}_{\text{derm-human}}}$$

sRV = standard respiratory volume

$\text{ABS}_{\text{inh – rat}}$ = 100%

$\text{ABS}_{\text{derm – Human}}$ = 10%

5,400 * 0.29 * 100 / 10 = 15,660 mg/kg bw/day

The dermal NOAEL is converted to internal dose taking into account 10% absorption via skin and compared to the systemic dose per day via skin for each scenario.

Result is summarised in table 4.45.

Sum of exposures

The internal dose of 321 mg/kg/d, corresponding to the NOAEC of 5400 mg/m^3 is compared with exposure estimate. Result is summarised in table 4.45:

Table 4.45: MOS and conclusion for fertility effects

SCENARIO	Inhalation		Dermal		Sum of exposures	
	MOS	Conclusion	MOS	Conclusion	MOS	Conclusion
1. AQUEOUS PAINTSAND FLOOR VARNISHES	535	ii	1566000	ii	535	ii
2. HOUSE CLEANERS	321	ii	22371	ii	189	ii

Conclusion ii is reached for all consumers scenarios.

Developmental toxicity

PGMA is not teratogenic. No effects were seen in foetuses without evident signs of maternal toxicity. It is concluded that PGMA is of no concern for consumers with regard to developmental toxicity (**conclusion ii**)

4.1.3.3.8 Summary of risk characterisation for consumers

Conclusion iii is reached for eye and respiratory tract irritation for house cleaners scenario, and for repeated dose toxicity local effects for aqueuous paints and floor varnishes and for house cleaners scenarios.
Conclusion ii is reached for all other consumers scenarios concerning all other toxicological end-points.

4.1.3.4 Humans exposed via the environment

The key health effects is repeated dose toxicity and reproductive toxicity (fertility effects). The other endpoints such as mutagenicity or carcinogenicity are not characterised since there are no concern for these effects. Comparison of the total internal dose of 96 mg.kg^{-1} (corresponding to the NOAEC of 1620 ppm for repeated dose toxicity via inhalation and calculated assuming respiratory volume of 20 m^3 a day and a mean human bw of 60 kg) with the highest estimated exposure at regional (1.67×10^{-4} mg.kg^{-1}.day^{-1}) and local (0.174 mg.kg^{-1}.day^{-1}) levels leads to margins of safety of, respectively, 5.75×10^5 and 552 which do not lead to concern (the reference MOS for repeated dose toxicity is 25). For fertility end-point, effects seen with PGME can be expected (see 2 generation study by inhalation route with PGME; 6h/day and 5 days a week). These effects led to a NOAEC of 1000 ppm (5400 mg/m^3 for PGMA) leading to a total internal dose of 321 mg/kg/d which leads to margin of safety of 1.92×10^6 and 1845 for regional and local levels. No concern is anticipated with a reference MOS for reproductive toxicity by inhalation of 25.

Summary of risk characterisation for exposure via the environment

Conclusion

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

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

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

PGMA has no explosive or oxidising properties but it is flammable (flash point is 42°C). Vapours can form flammable and explosive mixtures with air within the range of 1.5 to 12 % 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.

Conclusion ii.

5 RESULTS [6]

5.1 INTRODUCTION

5.2 ENVIRONMENT

5.3 HUMAN HEALTH

5.3.1 Human health (toxicity)

Acute toxicity of PGMA is low in rodents. This chemical is mildly irritating to eye, but not to skin. PGMA is not skin-sensitising in guinea pigs. For repeated dose toxicity, inhalation studies demonstrated that PGMA caused local irritation effect probably because of the hydrolysis *in situ* in PGME and acetate. Two bacterial mutation tests, unscheduled DNA synthesis in rat hepatocytes and chromosomal aberration test *in vitro* show negative results. An UDS study was also negative. No data is available for carcinogenicity. Cross-reading with PGME data is possible because of the rapid hydrolysis of PGMA to PGME and acetate. No carcinogenic properties are expected for PGME moiety and risk of seeing carcinogenic development due to the local irritation caused by the acetate moiety is taken into account by the RDT risk characterisation. PGMA did not produce any fertility effects in rats and there was no evidence of teratogenicity of PGMA.

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

Conclusion (ii) 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 end points and scenarios.

[6] Conclusion (i) There is a need for further information and/or testing.
Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

5.3.1.2 Consumers

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 is reached for eye and respiratory tract irritation for house cleaners scenario, and for repeated dose toxicity local effects for aqueous paints and floor varnishes and for house cleaners scenarios.

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

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.

5.3.1.3 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.

5.3.2 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.

6 REFERENCES

AISE, 2002 - Table of Habits and Practices for Consumer Products in Western Europe

Angerer J., Lichterbeck E., Begerow J., Sekel S. and Lehnert G, 1990. Occupational exposure to organic solvents - XIII. Glycolether exposure during the production of varnishes. *Int Arch Occup Environ Health* 62, 123-126.

Arbejdstilsynet, 2001. Danish product register. Letter dated April 11, 2001.

Auffarth J., Hohmann R. and Tischer M., 1998. Stoffbelastungen in Siebdruckereien. Schriftenreihe der Bundesanstalt für Arbeitsschutz und Arbeitsmedizin. GA 53, Dortmund/Berlin (90 pages).

BASF, 2001. Safety data sheet Methoxypropylacetat (PGMA). BASF. Ludwigshafen, Germany.

Ben-Brik E., Jérôme L., Arnaud I., Yous S., Labat L., Haguenoer J.M. and Multigner L., 2004. Exposure to glycols ethers in a population of French men evaluated by measurement of urinary alkoxycarboxylic acids. *Int Arch Occup Environ Health* 77, 368-372.

BGAA, 2001. 1-Methoxy-2-propanol acetate exposure at the workplace. Exposure characterisation no 44.

BP, 1998. Oxygenated solvents-Product technical information: Methoxypropanol Acetate. BP. United Kingdom.

BP,2000. Safety data sheet_methoxypropylacetate. BP chemicals.

BP, 2002. Letter (ref EB314): Exposure data from the screen printing industry.

CEPE,2002. Analysis of the answers to the questionnaire on the use of 1-methoxypropan-2-ol in paints and inks manufacturing industries. Document communicated by CEPE, february 2002.

Chemicals Evaluation and Research Institute, 1998. Report N°8(2) 3144 K. Kurume, Japan

Corley R.A., Gies R.A., Wu H. and Weitz K.K., 2005. Development of a PbPk pharmacokinetic model for PGME and its acetate in rats and humans. Toxicol. Letters, 156, 193-213.

Delgado P., Porcel J., Abril I., Torres N., Terán A. and Zugasti A. Potential Dermal Exposure during the Painting Process in Car Body Repair Shops, 2004. *Ann. Occup. Hyg.*, 48 (3), 229-236.

Dow Chemical Company, 1980. "DOWANOL® PGME Acetate: acute toxicological properties and industrial handling hazards", unpublished report.

Dow Chemical Company, 1983. "Evaluation of DOWANOL® PGME Acetate in the Ames Salmonella/mammalian microsomal mutagenicity assay", unpublished report.

Dow Chemical Company, 1985. "Propylene glycol monomethyl ether acetate: Inhalation uptake in rats and effects on respiration in rats and mice", unpublished report.

Dow Chemical Company,1985b. "Propylene glycol monomethyl ether acetate (DOWANOL® PGMA): skin sensitization study in the guinea pig", unpublished report.

Dow Chemical Company, 1985c. "Propylene glycol monomethyl ether acetate: inhalation uptake in rats and effects on respiration in rats and mice", unpublished report.

Dow Chemical Company, 1992. "Propylene glycol monomethyl ether acetate: acute toxicological studies in rats with cover letter dated 072492", EPS/OTS: Doc. #88-920005652. NTIS Order No.: NTIS/OTS 0544435.

Dow, 1993. Acute eye irritation study in rabbits with PGMA. R&D report.

Dow-France, 2001. Fiche de données de sécurité_Dowanol* PMA glycol ether acetate. Dow France SAS. Le Raspail, Paris Nord 2.

Dow Chemical Company, 2001. PGME and PGMEA: A. *in vitro* hydrolysis of PGMEA in rat and human blood and liver homogenate. B. Kinetics of PGME and PGMEA following intravenous administration to fisher 344 rats. Laboratory project study 001023.

Emmen H.H., Muijser H., Arts J.H.E. and Prinsen M.K., 2003. Human Volunteer Study with Propylene Glycol Monomethyl Ether: Eye irritation during vapour exposure. Toxicol. Letters, 140-141, 249-259.

FIPEC, 2001. Personnal communication.

Gijsbers J.H.J., Tielemans E., Brouwer D.H. and Van Hemmen J.J.,.2004. Dermal exposure during filling, loading and brushing with products containing 2-(2-butoxyethoxy)ethanol,. *Ann. Occup. Hyg.*, 48 (3), 219-227.

Gonsior S.J., 1990. Environmental Assessment for Glycol Ethers. The Dow Chemical Company. Midland, Michigan.

Hansch C. and Leo A., 1979. Substituent constants for correlation analysis in chemistry and biology. New York, p 352.

Hughson G.W., Aitken R.J., 2004. Determination of dermal exposures during mixing, spraying and wiping activities. *Ann. Occup. Hyg.*, 48 (3), 245-255.

INRS, 2002. Extractions from the SEPIA database for products containing PGMA Internal document of INRS.

KEMI, 2002. Information from the Swedish Product Register on 4th priority list substances (ESR 793/93), letter dated 04/19/02.

KRIOH,2003. Riskofderm Project QLK4-CT-1999-01107. Deliverable 41. Work part 3.

Laitinen J., 1998. Correspondence between occupational exposure limit and biological action level values for alkoxyethanols and their acetates. Int Arch Occup Environ Health 71, 117-124.

LYONDELL, 1999 - Material safety data sheet_Arcosolv PMA. Lyondell service center europe. Rotterdam, The Netherlands.

Maguire H. C., 1973, J. Soc. Cosm. Chem., 24, 151-162.

Mandrala, A. L., (1983) "Evaluation of DOWANOL® PGMAcetate in the rat hepatocyte UDS assay", unpublished report of the Dow Chemical Company.Marquart H., Warren N.D., Laitinen J., Van Hemmen J.J., 2006 – Default values for assessment of potential dermal exposure of the hands to industrial chemicals in the scope of regulatory risk assessments. *Ann. Occup. Hyg.,* 50, 469-489.

Ministry of Health & Welfare (Japan), 1998 - Toxicity Testing Reports of Environmental Chemicals vol.6 205-227 .

Miller R.R., Hermann E.A., Young J.T., Clahoun L.L. and Kastl P.E., 1984 - PGMEA metabolism, disposition, and short-term vapor inhalation toxicity studies. *Toxicol. Appl. Pharm*. 75, 521-530 .

Noakes and Sanderson, 1969. A method for determining the dermal toxicity of pesticides. *Brit. J. Industr. Med*., 26, 59-64.

Pearson N., 1986 - Methyl proxitol acetate : acute toxicity (*Salmo gairneri*, *Daphnia magna* and *Selenastrum capricornutum*) and N-octanol/water partition coefficient. SHELL. London, England.

RISKOFDERM, 2002a. Deliverable 29. Main study report of partner 1. TNO, The Netherlands.

RISKOFDERM, 2002b. Deliverable 34a. Main study report of partner 15. INSHT, Spain.

RISKOFDERM, 2002c. Deliverable 32. Main study report of partner 4. IOM, UK.

RISKOFDERM, 2003a. Deliverable 41. Benchmark study report of partner 2. KRIOH, Finland.

RISKOFDERM, 2003b. Project QLK4-CT-1999-01107. Deliverable 41. Work part 3. Responsible partner: KRIOH

Rowe V.K., MC Collister D.D., Spencer H.C., Oyen F. Hollingsworth R.L., Drill V.A., 1954 - Toxicology of mono-, di- and tripropylene glycol methyl ethers. *Am. Assoc. Arch. Ind. Hyg. Occup. Med.*, 9, 509-525

SHELL, 1985. Genotoxicity studies with methoxy proxitol acetate. Group research report SBGR.85.162.

SHELL, 1985b. Toxicology of ethylene oxide derivative: the acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitising potential of metyl proxitol acetate.

SHELL, 2000 - Safety Data Sheet_PGMA (Methyl Proxitol Acetate). SHELL.

SIDS initial assessment profile, 1996.

SIDS initial assessment report for 11th SIAM,2001. 1-Methoxypropan-2-ol acetate (PGMA). Sponsor country : Japon

Staples C.A. and Davis J.W.,2002 - An examination of the physical properties, fate, ecotoxicity and potential environmental risk for a series of propylene glycol ethers. Chemosphere, 49, 61-73.

Steward, R.D., Edward B.D., Dodd H.C., Torkelson T.R., 1970 - Experimental Human Exposure to Vapor of Propylene Glycol Monomethyl Ether. *Arch Environ Health,* 20**,** 218-223**.**

Sumner Susan C.J., 1999 Blood Pharmacokinetics of Propylene Glycol Methyl Ether (PGME) and Propylene Glycol Methyether Acetate (PGMEA) in Male F-344 Rats after Dermal Application, Final Report 98003.

Union Carbide Corporation, 1961, "Propylene glycol monoethyl ether acetate: (USAR) Solvent LM Acetate", unpublished report.U.S. Army Environmental Hygiene Agency (USAEHA), 1989 "Assessment of the developmental toxicity of propylene glycol monomethyl acetate (PM Acetate) in rats".

US EPA and Syracuse Research Corporation, 2001 EPI Suite*. US EPA,*

Vincent R., Rieger B., Subra I. and Poirot P., 1996. Exposure assessment to glycol ethers by atmosphere and biological monitoring. *Occup Hyg* 2, 79-90.

Vincent R., 1999. Exposition professionnelle (occupational exposure). *In*: Ethers de glycol, quels risques pour la santé ? Expertise collective, Ed. INSERM, pp. 237-256. (in French)

Vincent R. and Jeandel B., 1999. Evolution des niveaux d'exposition entre 1987 et 1998. *In*: Ethers de glycol, quels risques pour la santé ? Expertise collective, Ed. INSERM, pp. 257-262. (in French)

Vincent R., 2003. Actualisation des données d'exposition aux éthers de glycol dans COLCHIC : période 1999-2002.

Wesolowski W. and Gromiec J.P., 1997. Occupational exposure in polish paint and lacquer industry. *Internat J Occup Med Environ Health* 10(10), 79-88.

Zissu D., 1995 Contact Dermatitis, 32 74-77.

ABBREVIATIONS

[update the list to correspond to the substance RAR]

2MPA	2 methoxy propionic acid
ADI	Acceptable Daily Intake
AF	Assessment Factor
ASTM	American Society for Testing and Materials
ATP	Adaptation to Technical Progress
AUC	Area Under The Curve
B	Bioaccumulation
BBA	Biologische Bundesanstalt für Land- und Forstwirtschaft
BCF	Bioconcentration Factor
BMC	Benchmark Concentration
BMD	Benchmark Dose
BMF	Biomagnification Factor
bw	body weight / *Bw*, *b.w.*
C	Corrosive (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
CA	Chromosome Aberration
CA	Competent Authority
CAS	Chemical Abstract Services
CEC	Commission of the European Communities
CEN	European Standards Organisation / European Committee for Normalisation
CEPE	European council of paint printing and artists' colours industry.
CMR	Carcinogenic, Mutagenic and toxic to Reproduction
CNS	Central Nervous System
COD	Chemical Oxygen Demand
CSTEE	Scientific Committee for Toxicity, Ecotoxicity and the Environment (DG SANCO)
CT_{50}	Clearance Time, elimination or depuration expressed as half-life
d.wt	dry weight / dw
dfi	daily food intake
DG	Directorate General
DIN	Deutsche Industrie Norm (German norm)
DNA	DeoxyriboNucleic Acid
DOC	Dissolved Organic Carbon
DT50	Degradation half-life or period required for 50 percent dissipation / degradation
DT90	Period required for 50 percent dissipation / degradation

E	Explosive (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
EASE	Estimation and Assessment of Substance Exposure Physico-chemical properties [Model]
EbC50	Effect Concentration measured as 50% reduction in biomass growth in algae tests
EC	European Communities
EC10	Effect Concentration measured as 10% effect
EC50	median Effect Concentration
ECB	European Chemicals Bureau
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
ECVAM	European Centre for the Validation of Alternative Methods
EDC	Endocrine Disrupting Chemical
EEC	European Economic Communities
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EN	European Norm
EPA	Environmental Protection Agency (USA)
ErC50	Effect Concentration measured as 50% reduction in growth rate in algae tests
ESD	Emission Scenario Document
EU	European Union
EUSES	European Union System for the Evaluation of Substances [software tool in support of the Technical Guidance Document on risk assessment]
F(+)	(Highly) flammable (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
FAO	Food and Agriculture Organisation of the United Nations
FELS	Fish Early Life Stage
GLP	Good Laboratory Practice
HEDSET	EC/OECD Harmonised Electronic Data Set (for data collection of existing substances)
HELCOM	Helsinki Commission -Baltic Marine Environment Protection Commission
HPLC	High Pressure Liquid Chromatography
HPVC	High Production Volume Chemical (> 1000 t/a)
IARC	International Agency for Research on Cancer
IC	Industrial Category
IC50	median Immobilisation Concentration or median Inhibitory Concentration
ILO	International Labour Organisation
IPCS	International Programme on Chemical Safety
ISO	International Organisation for Standardisation
IUCLID	International Uniform Chemical Information Database (existing substances)
IUPAC	International Union for Pure and Applied Chemistry

JEFCA	Joint FAO/WHO Expert Committee on Food Additives
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
Koc	organic carbon normalised distribution coefficient
Kow	octanol/water partition coefficient
Kp	solids-water partition coefficient
L(E)C50	median Lethal (Effect) Concentration
LAEL	Lowest Adverse Effect Level
LC50	median Lethal Concentration
LD50	median Lethal Dose
LEV	Local Exhaust Ventilation
LLNA	Local Lymph Node Assay
LOAEL	Lowest Observed Adverse Effect Level
LOEC	Lowest Observed Effect Concentration
LOED	Lowest Observed Effect Dose
LOEL	Lowest Observed Effect Level
MAC	Maximum Allowable Concentration
MATC	Maximum Acceptable Toxic Concentration
MC	Main Category
MITI	Ministry of International Trade and Industry, Japan
MOE	Margin of Exposure
MOS	Margin of Safety
MW	Molecular Weight
N	Dangerous for the environment (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC
NAEL	No Adverse Effect Level
NOAEC	No Observable Adverse Effect Concentration
NOAEL	No Observed Adverse Effect Level
NOEL	No Observed Effect Level
NOEC	No Observed Effect Concentration
NTP	National Toxicology Program (USA)
O	Oxidizing (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
OECD	Organisation for Economic Cooperation and Development
OEL	Occupational Exposure Limit
OJ	Official Journal
OSPAR	Oslo and Paris Convention for the protection of the marine environment of the Northeast Atlantic
P	Persistent

PBT	Persistent, Bioaccumulative and Toxic
PBPK	Physiologically Based PharmacoKinetic modelling
PBTK	Physiologically Based ToxicoKinetic modelling
PEC	Predicted Environmental Concentration
pH	logarithm (to the base 10) (of the hydrogen ion concentration $\{H^+\}$
pKa	logarithm (to the base 10) of the acid dissociation constant
pKb	logarithm (to the base 10) of the base dissociation constant
PNEC	Predicted No Effect Concentration
POP	Persistent Organic Pollutant
PPE	Personal Protective Equipment
QSAR	(Quantitative) Structure-Activity Relationship
R phrases	Risk phrases according to Annex III of Directive 67/548/EEC
RAR	Risk Assessment Report
RC	Risk Characterisation
RfC	Reference Concentration
RfD	Reference Dose
RNA	RiboNucleic Acid
RPE	Respiratory Protective Equipment
RWC	Reasonable Worst Case
S phrases	Safety phrases according to Annex III of Directive 67/548/EEC
SAR	Structure-Activity Relationships
SBR	Standardised birth ratio
SCE	Sister Chromatic Exchange
SDS	Safety Data Sheet
SETAC	Society of Environmental Toxicology And Chemistry
SNIF	Summary Notification Interchange Format (new substances)
SSD	Species Sensitivity Distribution
STEL	Shot term exposure limit
STP	Sewage Treatment Plant
T(+)	(Very) Toxic (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
TDI	Tolerable Daily Intake
TG	Test Guideline
TGD	Technical Guidance Document
TNsG	Technical Notes for Guidance (for Biocides)
TNO	The Netherlands Organisation for Applied Scientific Research
TWA	Time weighted average
UC	Use Category

UDS	Unscheduled DNA Synthesis
UN	United Nations
UNEP	United Nations Environment Programme
US EPA	Environmental Protection Agency, USA
UV	Ultraviolet Region of Spectrum
UVCB	Unknown or Variable composition, Complex reaction products of Biological material
vB	very Bioaccumulative
vP	very Persistent
vPvB	very Persistent and very Bioaccumulative
v/v	volume per volume ratio
w/w	weight per weight ratio
WHO	World Health Organization
WWTP	Waste Water Treatment Plant
Xn	Harmful (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
Xi	Irritant (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)

APPENDIX A

Methods of calculation of consumer exposures

Scenario 2 : Aqueous paints and floor varnishes

WALLPAINT EXPOSURE MODEL (WPEM)

Resident DIY model

Room volume 25m^3

Painted area 28m^2

Air changes 0.5 per hour

Paint quantity:5kg, density 1.3, type: flat

Model type: empirical

Body mass: 60kg

Events per year: 10

Active/total lifetime: 40/70 years

No sinks

PGMA content: 20%

Painting time: 133 minutes

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