

Screening Assessment for the Challenge

Ethanol, 2-(2-methoxyethoxy)-

**Chemical Abstracts Service Registry Number
111-77-3**

**Environment Canada
Health Canada**

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Synopsis

Pursuant to section 74 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999), the Ministers of the Environment and of Health have conducted a screening assessment of ethanol, 2-(2-methoxyethoxy)- (diethylene glycol monomethyl ether, DEGME), Chemical Abstracts Service Registry Number 111-77-3. The substance DEGME was identified in the categorization of the *Domestic Substances List* as a high priority for action under the Ministerial Challenge. DEGME was identified as a high priority because it was considered to pose greatest potential for exposure of individuals in Canada and had been classified by the European Commission on the basis of developmental toxicity. The substance did not meet the ecological categorization criteria for persistence, bioaccumulation potential or inherent toxicity to aquatic organisms. Therefore, the focus of this assessment of DEGME relates principally to human health risks.

According to information reported under section 71 of CEPA 1999, DEGME was imported into Canada in 2006 in a quantity ranging between 1 000 000 and 10 000 000 kg. DEGME has various applications, including use as an additive in jet fuel and as a solvent in paints and is used in various products such as floor care products, brake fluid and some skin creams and cleansers.

Based on limited information on concentrations in environmental media and results from a survey under section 71 of CEPA 1999, exposure of the general population via the environment is expected to be low. However, exposure to DEGME by inhalation and dermal contact may occur during use of products that contain the substance. The health effects associated with exposure to DEGME are primarily developmental and reproductive toxicity and hematological effects, based on observations in experimental animals. The margins between the upper bounding estimates of dermal exposure to DEGME from consumer products, taking into consideration frequencies of use and the critical effect levels, particularly for developmental toxicity, in short-term or subchronic studies in experimental animals, may not be adequately protective. Although the margin between measured indoor air concentrations and the concentration at which no effects were observed in experimental animals (the highest concentration tested) is large, in light of the lack of an inhalation study for developmental toxicity, which appears to be the most sensitive effect, data are considered inadequate to characterize risk to health associated with exposure to DEGME by inhalation while using consumer products containing this substance.

On the basis of the potential inadequacy of the margins between conservative estimates of exposure to DEGME by dermal contact during use of consumer products and critical effect levels, particularly for developmental toxicity, in experimental animals, it is concluded that DEGME be considered a substance that is entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

On the basis of low ecological hazard, expected releases and low environmental exposure of DEGME, it is concluded that this substance is not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends. DEGME does not meet the criteria for persistence or bioaccumulation as set out in the *Persistence and Bioaccumulation Regulations*.

This substance will be included in the upcoming *Domestic Substances List* inventory update initiative. In addition and where relevant, research and monitoring will support verification of assumptions used during the screening assessment and, where appropriate, the performance of potential control measures identified during the risk management phase.

Based on the information available, DEGME meets one or more of the criteria set out in section 64 of CEPA 1999.

Introduction

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) (Canada 1999) requires the Minister of the Environment and the Minister of Health to conduct screening assessments of substances that have met the categorization criteria set out in the Act to determine whether these substances present or may present a risk to the environment or to human health. Based on the results of a screening assessment, the Ministers can propose to take no further action with respect to the substance, to add the substance to the Priority Substances List for further assessment or to recommend that the substance be added to the List of Toxic Substances in Schedule 1 of the Act and, where applicable, the implementation of virtual elimination.

Based on the information obtained through the categorization process, the Ministers identified a number of substances as high priorities for action. These include substances that

- met all of the ecological categorization criteria, including persistence (P), bioaccumulation potential (B) and inherent toxicity to aquatic organisms (iT), and were believed to be in commerce; and/or
- met the categorization criteria for greatest potential for exposure (GPE) or presented an intermediate potential for exposure (IPE) and had been identified as posing a high hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity.

The Ministers therefore published a notice of intent in the *Canada Gazette*, Part I, on December 9, 2006 (Canada 2006), which challenged industry and other interested stakeholders to submit, within specified timelines, specific information that may be used to inform risk assessment and to develop and benchmark best practices for the risk management and product stewardship of those substances identified as high priorities.

The substance ethanol, 2-(2-methoxyethoxy)- (diethylene glycol monomethyl ether, referred to as DEGME), was identified as a high priority for assessment of human health risk because it was considered to present GPE and had been classified by another agency on the basis of developmental toxicity.

The Challenge for DEGME was published in the *Canada Gazette* on August 18, 2007 (Canada 2007). A substance profile was released at the same time. The substance profile presented the technical information available prior to December 2005 that formed the basis for categorization of this substance. As a result of the Challenge, submissions of information were received.

Although DEGME was determined to be a high priority for assessment with respect to human health, it did not meet the criteria for persistence, bioaccumulation potential or

inherent toxicity to aquatic organisms. Therefore, this assessment focuses principally on information relevant to the evaluation of risks to human health.

Under CEPA 1999, screening assessments focus on information critical to determining whether a substance meets the criteria for defining a chemical as “toxic” as set out in section 64 of the Act, where

64. [...] a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions that
- (a) have or may have an immediate or long-term harmful effect on the environment or its biological diversity;
 - (b) constitute or may constitute a danger to the environment on which life depends; or
 - (c) constitute or may constitute a danger in Canada to human life or health.

Screening assessments examine scientific information and develop conclusions by incorporating a weight of evidence approach and precaution.

This screening assessment includes consideration of information on chemical properties, hazards, uses and exposure, including the additional information submitted under the Challenge. Data relevant to the screening assessment of this substance were identified in original literature, review and assessment documents and stakeholder research reports and from recent literature searches, up to June 2008 for the exposure section of the document and up to October 2007 for the health effects section. Key studies were critically evaluated; modelling results may have been used to reach conclusions. Evaluation of risk to human health involves consideration of data relevant to estimation of exposure (non-occupational) of the general population, as well as information on health hazards (based principally on the weight of evidence assessments of other agencies that were used for prioritization of the substance). Decisions for human health are based on the nature of the critical effect and/or margins between conservative effect levels and estimates of exposure, taking into account confidence in the completeness of the identified databases on both exposure and effects, within a screening context. The screening assessment does not represent an exhaustive or critical review of all available data. Rather, it presents a summary of the critical information upon which the conclusion is based.


This screening assessment was prepared by staff in the Existing Substances Programs at Health Canada and Environment Canada and incorporates input from other programs within these departments. This assessment has undergone external written peer review/consultation. Comments on the technical portions relevant to human health were received from scientific experts selected and directed by Toxicology Excellence for Risk Assessment (TERA), including Susan Griffin (US Environmental Protection Agency Region 8), Michael Jayjock (The Lifeline Group) and Joan Strawson (TERA). Comments on these sections were also received from ToxEcology Environmental Consulting Ltd. Additionally, the draft of this screening assessment was subject to a 60-day public comment period. Although external comments were taken into consideration, the final content and outcome of the screening risk assessment remain the responsibility of Health Canada and Environment Canada.

The critical information and considerations upon which the assessment is based are summarized below.

Substance Identity

For the purposes of this document, this substance will be referred to as diethylene glycol monomethyl ether (DEGME).

Table 1. Substance identity of DEGME

CAS RN	111-77-3
DSL name	Ethanol, 2-(2-methoxyethoxy)-
NCI names	Diethylene glycol monomethyl ether (PICCS) Ethanol, 2-(2-methoxyethoxy)- (AICS, ASIA-PAC, ENCS, NZIoC, PICCS, SWISS, TSCA) Heptan-1-ol, 3,6-dioxa- (PICCS) Methoxydiethyleneglycol (PICCS) 2-(2-Methoxyethoxy)ethanol (ECL, EINECS, PICCS) 2-(2-Methoxy-ethoxy)ethanol (PICCS) 2-(2-Methoxy ethoxy)ethanol (PICCS) Methyl carbitol (PICCS) Methyl digol (PICCS)
Other names	Diethylene glycol methyl ether; Diethylene glycol monoethyl ether; Diethylene glycol monomethyl ether; Diglycol monomethyl ether; Dowanol DM; Ektasolve DM; Ethanol, 2,2'-oxybis-, monomethyl ether; Hicotol CAR; Hisolve DM; 2-Hydroxyethyl 2-methoxyethyl ether; Methoxydiglycol; 2-(2'-Methoxyethoxy)ethanol; 2-(2-Methoxyethoxy)ethan-1-ol; Methyl diethylene glycol; Methyl dioxitol
Chemical group (DSL stream)	Organics
Chemical subgroup	Glycol ethers
Chemical formula	C ₅ H ₁₂ O ₃
Chemical structure	
SMILES	O(CCOC)CCO
Molecular mass	120.15 g/mol

Abbreviations: AICS, Australian Inventory of Chemical Substances; ASIA-PAC, Asia-Pacific Substances Lists; CAS RN, Chemical Abstracts Service Registry Number; DSL, Domestic Substances List; ECL, Korean Existing Chemicals List; EINECS, European Inventory of Existing Commercial Chemical Substances; ENCS, Existing and New Chemical Substances; NCI, National Chemical Inventories; NZIoC, New Zealand Inventory of Chemicals; PICCS, Philippine Inventory of Chemicals and Chemical Substances; SMILES, simplified molecular input line entry specification; SWISS, Swiss Giftliste 1 and Inventory of Notified New Substances; TSCA, Toxic Substances Control Act Chemical Substance Inventory.

Source: NCI 2007

Physical and Chemical Properties

Table 2 summarizes the experimental and modelled physical and chemical properties of DEGME that are relevant to its environmental fate.

Table 2. Physical and chemical properties of DEGME¹

Property	Type	Value	Temperature (°C)	Reference
Melting point (°C)	Experimental	<-84		PhysProp 2006
Boiling point (°C)	Experimental	193		PhysProp 2006
Vapour pressure (Pa)	Experimental	24.0 (0.18 mmHg) ²	25	Daubert and Danner 1989
Henry's Law constant (Pa·m ³ /mol)	Experimental	6.59×10^{-5} (6.5×10^{-10} atm·m ³ /mol) ²	25	Hine and Mookerjee 1975
Log K _{ow} (dimensionless)	Modelled	-1.18	25	KOWWIN 2000
	Modelled	-1.156	25	ACD 2007
Log K _{oc} (dimensionless)	Modelled	0	25	PCKOCWIN 2000
	Modelled	0.7	25	ACD 2007
Water solubility (mg/L)	Experimental	1 000 000	15–25	Riddick et al. 1985
pK _a (dimensionless)	Modelled	14.36	25	ACD 2007

Abbreviations: K_{oc}, organic carbon partition coefficient; K_{ow}, octanol–water partition coefficient; pK_a, acid dissociation constant.

¹ Some of the physical and chemical properties in the table were generated using quantitative structure–activity relationship (QSAR) models.

² Values in parentheses are the values given in the original papers.

Sources

DEGME does not occur naturally in the environment. It is produced by reacting ethylene oxide and methanol with an alkali catalyst (EURAR 2000).

Based on a survey conducted under section 71 of CEPA 1999, no Canadian companies reported manufacturing DEGME in a quantity greater than or equal to the 100 kg reporting threshold in 2006. However, results from the same survey and from voluntary data submitted by industry indicated that the total quantity of DEGME imported into Canada in 2006 ranged from 1 million to 10 million kilograms (Environment Canada 2008a, b). According to Chinn et al. (2007), Canadian imports of DEGME come primarily from the United States.

Uses

According to submissions made under section 71 of CEPA 1999, the majority of DEGME is used as an additive in jet fuel (Environment Canada 2008a). It is also used as a

formulant in pest control products used in various applications, including the pulp and paper industry (PMRA 2007; Environment Canada 2008a). It is used as a solvent in floor finishes, in various cleaners and degreasers and in paints (Environment Canada 2008a). In addition, DEGME is used in various other applications and settings that would not result in exposure of the general population of Canada (Environment Canada 2008a). DEGME is also used as a solvent or viscosity decreasing agent (Winter 2005; CTFA 2008) in some hairsprays, skin creams and cleansers (CNS 2008), as well as a component of fragrances (CTFA 2008). Furthermore, this substance may be used as a solvent in the manufacture of inks and can end coatings used in food contact applications. However, the potential daily intake from this latter use is considered to be negligible, as the coating is cured, resulting in evaporation of the solvent (2008 personal communication from Food Packaging Materials and Incidental Additives Section, Food Directorate, Health Canada, to Existing Substances Bureau, Health Canada; unreferenced). According to the same source, DEGME has been used in cleaners used in the food industry; however, the surfaces that come into direct contact with food must be thoroughly rinsed with potable water; as well, non-food contact surfaces (e.g., floors) must be cleaned under well-ventilated conditions. Thus, population exposure from this use is also expected to be negligible.

DEGME is also used as a chemical intermediate (Lewis 2007); as a metal solvent for mineral oil soap and mineral oil-sulfonated oil mixtures; as a solvent for dyes, nitrocellulose, resins and lacquers; for setting the twist and conditioning of yarns and cloth (EURAR 2000); as a component of hydraulic fluids (Verschueren 2001; Lewis 2007); as a solvent for solvent-based silk screen printing inks, stamp pad inks, and ballpoint and felt tip writing pen inks; as a component for pastes used in printing cellulose acetate and polyester fabrics; as a solvent and coupling agent for vat dyeing fabrics; in rust removers, aluminum brighteners and paint and varnish removers (Dow Chemical 2004); in water- and solvent-based paints and varnishes; as a component of floor cleaners, sealants and polishes; and in windshield washer fluid (EURAR 2000; HPD 2008). It is also used as a coupling agent for making miscible organic-aqueous systems and as a raw material for plasticizers (EURAR 2000). Finally, DEGME is used as a deactivator and stabilizer for agricultural formulations used before crops emerge from the soil (Dow Chemical 2004; US EPA 2006) and as a solvent for pharmaceutical manufacturing (EURAR 2000).

Releases to the Environment

Information reported under section 71 of CEPA 1999 indicated that, in 2006, only 0.1 kg of DEGME was released to land and between 10 000 and 100 000 kg were released into water; between 10 000 and 100 000 kg were also released to air (Environment Canada 2008a). Most of the releases into air come from diffuse sources rather than from a single point source, so the resulting concentrations of DEGME in air would be low. Dispersive releases may also occur as a result of consumer and commercial uses of the substance.

Releases of DEGME are not currently reported to the National Pollutant Release Inventory (NPRI 2006) or to the US Toxics Release Inventory (TRI 2006).

Environmental Fate

As indicated in Table 2, DEGME has a very high water solubility (1 000 000 mg/L), a moderate vapour pressure (24.0 Pa), a very low Henry's Law constant ($6.59 \times 10^{-5} \text{ Pa}\cdot\text{m}^3/\text{mol}$), a very low $\log K_{ow}$ (<0) and a very low $\log K_{oc}$ (0–0.7). These properties suggest that if DEGME were to be released into the environment, it would be expected to be found in water.

Based on its physical and chemical properties (Table 2) and the results of Level III fugacity modelling (Table 3), DEGME is expected to reside predominantly in water or in soil, depending on the compartment of release. Based on information provided above, release of this substance to soil is not typical. In addition, although there are potentially releases of DEGME to air, which could result in partitioning to soil, this substance is not persistent in soil and therefore not likely to remain in this compartment.

Table 3. Results of Level III fugacity modelling (EQC 2003) for DEGME

Substance released to:	Fraction of substance partitioning to each medium (%)			
	Air	Water	Soil	Sediment
Air (100%)	2.5	27.5	69.9	0.05
Water (100%)	0.0001	99.8	0.003	0.17
Soil (100%)	0.02	22.2	77.8	0.04

Persistence and Bioaccumulation Potential

Environmental Persistence

When released into the environment, DEGME is not expected to be persistent in air, water, soil or sediment.

Modelled data for the persistence of DEGME in air and water are shown in Table 4.

Table 4. Modelled data for persistence of DEGME in the environment

Fate process	Degradation value	Endpoint (units)	Reference
Atmospheric oxidation	0.41	$t_{1/2}$ (days)	AOPWIN 2000
Biodegradation in water	15	$t_{1/2}$ (days)	BIOWIN 2000 (Ultimate Survey Model)
	0.8298	Probability	BIOWIN 2000 (MITI Non-Linear)

Abbreviations: MITI, Ministry of International Trade & Industry, Japan; $t_{1/2}$, half-life.

Using an extrapolation ratio of 1:1:4 for a water:soil:sediment biodegradation half-life (Boethling et al. 1995), the half-life in soil is <182 days and the half-life in sediments is

<365 days. This indicates that DEGME is not expected to be persistent in soil or sediment.

The weight of evidence based on the data described above indicates that DEGME does not meet the persistence criteria for air (half-life in air ≥ 2 days), water or soil (half-life in water or soil ≥ 182 days) or sediment (half-life in sediment ≥ 365 days), as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Potential for Bioaccumulation

Modelled data for the bioaccumulation potential of DEGME, presented in Table 5, indicate that DEGME does not meet the bioaccumulation criteria (BCF, BAF ≥ 5000) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Table 5. Modelled data for bioaccumulation of DEGME in fish

Endpoint	Value (L/kg wet weight)	Reference
BAF	1	Arnot and Gobas 2003 (Modified Gobas BAF)
BCF	1	Arnot and Gobas 2003 (Modified Gobas BCF)
BCF	1.0	ACD 2007
BCF	9.16	OASIS Forecast 2005
BCF	3.16	BCFWIN 2000

Abbreviations: BAF, bioaccumulation factor; BCF, bioconcentration factor.

Potential to Cause Ecological Harm

As indicated previously, DEGME does not meet the persistence or bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

There is modelled and experimental evidence indicating that DEGME does not cause harm to aquatic organisms at relatively low concentrations (i.e., does not exhibit acute LC₅₀/EC₅₀ values of ≤ 1.0 mg/L) but rather has low acute toxicity. A study on the acute aquatic toxicity of DEGME to the fish *Carassius auratus* resulted in an LC₅₀ of >5000 mg/L (Bridié et al. 1979). This value is supported by the predictions of most models, shown in Table 6.

Table 6. Modelled data for toxicity of DEGME in aquatic organisms

Test organism	Type of test	Endpoint	Value (mg/L)	Reference
Green alga	Chronic	96-h MATC	619.2	ECOSAR 2004
Green alga	Chronic	96-h EC ₅₀	38 906.5	ECOSAR 2004
<i>Daphnia magna</i>	Acute	48-h EC ₅₀	40.4	TOPKAT 2004
Daphnid	Subacute	16-day EC ₅₀	953.5	ECOSAR 2004
Daphnid	Acute	48-h EC ₅₀	74 734.8	ECOSAR 2004
Mysid shrimp	Acute	96-h LC ₅₀	243 000	ECOSAR 2004
Fathead minnow, <i>Pimephales promelas</i>	Acute	96-h LC ₅₀	17 200	TOPKAT 2004

Test organism	Type of test	Endpoint	Value (mg/L)	Reference
Fathead minnow, <i>Pimephales promelas</i>	Acute	96-h LC ₅₀	28 370.6	AIES 2003–2005
Fathead minnow, <i>Pimephales promelas</i>	Acute	96-h LC ₅₀	1 226 563.1	OASIS Forecast 2005
Fish	Subacute	30-day MATC	6703.8	ECOSAR 2004
Fish	Acute	14-day LC ₅₀	94 951.7	ECOSAR 2004
Fish	Acute	96-h LC ₅₀	4276.8	ECOSAR 2004
Fish	Acute	96-h LC ₅₀	86 880.6	ECOSAR 2004

Abbreviations: EC₅₀, concentration affecting 50% of the test population; LC₅₀, lethal concentration affecting 50% of the test population; MATC, maximum acceptable toxicant concentration.

Environmental releases of DEGME to air and water were reported under section 71 of CEPA 1999 (see “Releases to the Environment” above). Aquatic concentrations resulting from these releases were estimated. Environment Canada’s Industrial Generic Exposure Tool – Aquatic (IGETA) was employed to estimate the (worst-case) substance concentration in a generic watercourse receiving industrial effluents (Environment Canada 2008c). The generic scenario is designed to provide these estimates based on conservative assumptions regarding the amount of chemical processed and released, the number of processing days, the sewage treatment plant removal rate and the size of the receiving watercourse. However, according to the reporting company, the releases to water were actually releases to a treatment facility that is believed to remove virtually all of the substance before release into the river that receives effluent from the facility. The tool models an industrial release scenario based on loading data from sources such as industrial surveys and knowledge of the distribution of industrial discharges in the country and calculates a predicted environmental concentration (PEC). The equation and inputs used to calculate the PEC in the receiving watercourse are described in Environment Canada (2008d). Assuming a release of 6300 kg (the highest reported release to water for a facility reported under the section 71 survey), the obtained PEC was 0.7045 mg/L for point source releases.

To derive a predicted no-effects concentration (PNEC), the acute toxicity value of greater than 5000 mg/L from the Bridié et al. (1979) study cited above was divided by an assessment factor of 1000 to account for interspecies and intraspecies variability in sensitivity, to estimate a long-term no-effects concentration from a short-term LC₅₀ and to account for uncertainty in laboratory to field extrapolation. This gave a PNEC of 5 mg/L.

The resulting risk quotient (PEC/PNEC) is $0.7045/5 = 0.14$. Because the risk quotient is <1 , it is considered unlikely that industrial releases of DEGME would cause harm to aquatic organisms.

There are also releases of DEGME to air, but the sources tend to be diffuse, and the resulting atmospheric concentrations would be low. Furthermore, the substance is not persistent in air, so it is unlikely to accumulate to levels that would cause harm to terrestrial organisms.

Based on the information available, DEGME is unlikely to be causing ecological harm in Canada.

Uncertainties in Evaluation of Ecological Risk

Quantitative structure–activity relationship (QSAR) models were used to estimate persistence and bioaccumulation. There are uncertainties associated with the use of QSAR models to estimate these characteristics. In addition, the value for K_{ow} , which is used as input to the QSAR models, also had to be estimated.

Potential to Cause Harm to Human Health

Exposure Assessment

Measured concentrations of DEGME in environmental media in Canada were not available. DEGME was detected in drinking water in the United States; however, no concentration data were presented (US EPA 1984). Therefore, ChemCAN (2003) was used to predict average concentrations of DEGME in ambient air, water and soil. The amount of DEGME released and the media into which it was released were obtained from industrial data submitted through the section 71 survey (Environment Canada 2008a).

A maximum indoor air concentration of DEGME of $164 \mu\text{g}/\text{m}^3$ (mean of $0.6 \mu\text{g}/\text{m}^3$, with a detection limit of $5 \mu\text{g}/\text{m}^3$) was measured in Berlin, Germany, based on measurements from 400 rooms in 200 apartments (Plieninger and Marchl 1999). Schleibinger et al. (2001) also conducted an indoor air study in Berlin and reported a maximum indoor air concentration of $39 \mu\text{g}/\text{m}^3$ (mean of $<5 \pm 4 \mu\text{g}/\text{m}^3$, no detection limit identified) from 90 samples taken in residential homes and various public indoor environments between 1989 and 1999. The maximum value from the Schleibinger et al. (2001) study was chosen over that reported in Plieninger and Marchl (1999), as the maximum value from this latter study was much larger than the reported 95th-percentile value of $0.4 \mu\text{g}/\text{m}^3$ and likely not a typical concentration found in indoor environments.

Appendix 1 presents upper-bounding estimates of intake of DEGME for each age group in the general population of Canada, based on the limited information listed above. The upper-bounding estimate of daily intake for the general Canadian population ranges from $6.8 \mu\text{g}/\text{kg}$ of body weight (kg-bw) per day for seniors (aged 60 years and older) to $20.5 \mu\text{g}/\text{kg-bw}$ per day for toddlers (aged 6 months to 4 years), with intakes from indoor air representing the predominant source of exposure. Exposures from ambient air, water and soil are considered negligible in comparison. These indoor air exposures likely arise as a result of the use of certain consumer products containing DEGME inside the home.

A summary of upper-bounding dermal and inhalation exposure estimates, predicted using ConsExpo software, version 4.1 (ConsExpo 2006), for users of several consumer products is presented in Tables 7 and 8, respectively. The detailed calculations for the various products, including paint, paint remover, sealants and caulking, floor cleaner,

floor sealant, floor polish and brake fluid, are described in Appendix 2. A variety of other consumer products were listed in the Uses section above, such as ballpoint and felt tip pen inks and windshield washer fluid; however, insufficient data are available with which to derive estimates for all potential consumer products. In addition, these uses are expected to result in lower exposures compared with those described here.

Table 7. Summary of predicted dermal exposures to DEGME during use of selected consumer products¹ using ConsExpo, version 4.1 (ConsExpo 2006) (see Appendix 2)

Products	Acute applied dose (mg/kg-bw per event)	Chronic applied dose (mg/kg-bw per day)
Latex paint	2.5	
Floor polish	4.7	
Floor sealer	11	
Paint stripper/remover	0.56	
Floor cleaner (mixing and loading plus application)	0.68	0.19

¹ Acute estimates are shown for products that are used infrequently throughout the year (i.e., once or twice a year), whereas chronic estimates are shown for products that are used more frequently (i.e., every day or every week).

Table 8. Summary of predicted inhalation exposures to DEGME during use of selected consumer products using ConsExpo, version 4.1 (ConsExpo 2006) (see Appendix 2)

Products	Mean event concentration (mg/m ³)
Paint stripper/remover	588
Sealant/caulking	135
Latex paint	42
Floor polish	12
Floor sealer	11
Floor cleaner (mixing, loading and application)	8.9

For products used infrequently, exposure to DEGME through dermal contact is predicted to range up to approximately 11 mg/kg-bw per event (for floor sealer), whereas airborne concentrations during application could be as high as 588 mg/m³ (for paint stripper/remover). For products used more frequently, such as floor cleaners, dermal exposure is modelled to be approximately 0.19 mg/kg-bw per day, whereas airborne concentrations are predicted to be about 9 mg/m³.

DEGME is also found in some personal care products, such as skin cream, skin cleanser and hairspray (Table 9) (CNS 2008). Based on available data, aggregate dermal exposure to these products was estimated to total about 0.27 mg/kg-bw per day using the ConsExpo software, version 4.1 (ConsExpo 2006). Detailed calculations for this estimate are shown in Appendix 2. Inhalation exposure was estimated only for the hairspray scenario, as suggested by the model, and the predicted mean event concentration during use of hairspray was 0.0014 mg/m³—i.e., much lower than the concentrations from use of the products listed in Table 8.

Table 9. Summary of predicted dermal exposure estimates for personal care products using ConsExpo, version 1 (ConsExpo 2006) (see Appendix 2)

Products	Chronic applied dose (mg/kg-bw per day)
Body cream	0.23
Face cream	0.023
Facial cleanser	0.0071
Hairspray	0.01
Total	0.27

Confidence in the exposure database is considered to be low, as only two studies were identified on concentrations of DEGME in indoor air (neither of which was from Canada), and modelling was used to determine upper-bounding estimates for ambient air, water and soil. No studies were identified regarding the presence of this substance in food. Based on the physical and chemical properties, release information and use pattern, this substance is not likely to be found in soil or food. The predicted concentrations of DEGME in environmental media presented in Appendix 1 were based on the upper end of the reporting range for releases into the environment; thus, these values likely overestimate intakes, and actual exposures are probably significantly lower. There is also low confidence in the modelled estimates of exposure from consumer products. However, as these estimates are conservative, confidence is high that actual exposure levels do not exceed these levels. In contrast, due to the possible presence of DEGME in fragrances and other personal care products in which it is used as a viscosity decreasing agent and solvent, exposure may be underestimated.

Health Effects Assessment

The available health effects information for DEGME is summarized in Appendix 3.

The European Commission has classified DEGME as a Category 3 substance, with risk phrase R63 (“possible risk of harm to the unborn child”) (ESIS 2007). This classification was based on observed developmental effects, including fetal visceral and skeletal variations and/or malformations, and reduced pup survival abilities in various experimental animal species/strains after oral or dermal exposure to DEGME (EURAR 2000).

Developmental effects were observed in rodents orally exposed to DEGME. In Wistar rats, such effects included significantly increased incidence of fetal visceral variations in the thymus, delayed ossification in sternbrae and vertebrae and significantly decreased fetal body weights, in the absence of maternal toxicity, at 600 mg/kg-bw per day. At higher doses, more severe developmental effects, including significantly increased fetal resorptions, fetal visceral malformations in the cardiovascular system, higher incidence of variations in thymus and kidneys, fetal external malformations, fetal skeletal variations in ribs and vertebrae, reduced pup postnatal survival and further delayed ossification, were observed in the presence of maternal toxicity. Effects noted in dams included significantly decreased thymus weight, body weight gain and food consumption. The no-observed-(adverse-)effect levels (NO(A)ELs) for maternal toxicity and fetotoxicity were

600 and 200 mg/kg-bw per day, respectively (Yamano et al. 1993). The thymus appeared to be the most sensitive target organ in both dams and fetuses. Although the visceral malformations observed in Wistar rats were also noted in Sprague-Dawley rats following oral exposure to a comparable dose of DEGME (720 mg/kg-bw per day), more severe skeletal malformations (primarily in the ribs) were observed in the latter (Hardin et al. 1986), which suggested a strain difference. Additionally, significantly reduced pup viability was observed in orally exposed mice in the Chernoff/Kavlock assay (Schuler et al. 1984).

Dermal exposure to DEGME resulted in developmental toxicity in rabbits. At doses that did not induce maternal effects, developmental effects, including significantly delayed ossification in the fetal skull and cervical vertebrae, were observed in New Zealand White rabbits at 250 mg/kg-bw per day. At higher dose levels, a significantly increased incidence of fetal alterations, significantly delayed ossification in sternbrae and increased fetal resorptions were observed, accompanied by maternal effects, including significantly decreased red blood cell counts and packed cell volume, as well as significantly decreased body weight gain during gestation days 9–11. No developmental effects were observed at 50 mg/kg-bw per day (Dow Chemical 1983a, b; Scortichini et al. 1986).

No data on the potential developmental toxicity via inhalation exposure to DEGME were identified.

Effects on the male reproductive system induced by DEGME were observed in orally exposed rodents. Significantly reduced relative testes weights were observed at 2000 mg/kg-bw per day in a 20-day gavage study in rats (Kawamoto et al. 1990). In a 6-week gavage study in rats, testicular atrophy and altered sperm production were observed at 3600 mg/kg-bw per day, along with significantly reduced absolute and relative testes weights. No effects were observed at 900 mg/kg-bw per day (Krasavage and Vlaovic 1982). In addition, slightly reduced testicular weights were observed in mice administered 4000 mg DEGME/kg-bw per day in drinking water for 25 days (Nagano et al. 1984).

Oral administration of DEGME to experimental animals also significantly altered hematological parameters and various organ weights, such as decreased relative pituitary gland and thymus weights, along with lymphocyte depletion in the thymus cortex, and increased relative liver, kidney or heart weights (Krasavage and Vlaovic 1982; Nagano et al. 1984; Hardin et al. 1986; Kawamoto et al. 1990, 1992; Yamano et al. 1993). Upon consideration of available data, the European Commission (EURAR 2000) determined an overall oral NO(A)EL for such effects of 900 mg/kg-bw per day. No more recent data have been identified thus far to indicate any lower effect level. In the repeated dermal exposure studies in experimental animals, toxicological changes in liver and altered hematological and urinary parameters were also observed. The European Commission (EURAR 2000) established a conservative “marginal” dermal effect level (lowest dermal lowest-observed-effect level [LOEL]) of 40 mg/kg-bw per day, based on slight histopathological changes in the liver and elevated urinary calcium levels in a 13-week

study in guinea pigs (Hobson et al. 1986). Additionally, effects on blood and body weight of exposed dams were observed in the above-mentioned developmental toxicity study in rabbits (lowest-observed-(adverse-)effect level [LO(A)EL] was 750 mg/kg-bw per day) (Scortichini et al. 1986). In the only available subchronic inhalation study, no exposure-related effects on body weights, organ weights, hematological analyses, clinical chemistry analyses, urinalyses and gross and histopathological examinations were observed in rats at the highest concentration tested (216 ppm, equivalent to 1060 mg/m³) for 90 days (Miller et al. 1985).

With regard to potential carcinogenicity or chronic effects of DEGME, no animal or human data are available. As to the genotoxic potential of DEGME, although the database is somewhat limited, DEGME did not show mutagenicity or clastogenicity *in vitro*, with or without metabolic activation, in bacteria (Ames test) (ICI 1980; BASF AG 1989) and in cultured mammalian cells (chromosomal aberration test) (Müller 1997). The European Commission stated that DEGME is not considered to be mutagenic, and the effects observed in the repeated-dose toxicity studies do not give cause for concern for its carcinogenicity (EURAR 2000).

The confidence in the toxicity dataset is moderate, as experimental data are available for developmental toxicity, reproductive toxicity, repeated-dose toxicity, genetic toxicity and acute toxicity. However, some of the studies were not performed according to current standards (EURAR 2000).

Characterization of Risk to Human Health

Based principally on the weight of evidence classification of DEGME by the European Commission as a Category 3 substance due to its developmental toxicity (ESIS 2007) and an assessment prepared by the European Union (EURAR 2000), as well as consideration of the available relevant data, the critical effects for characterization of risk to human health for DEGME are developmental and reproductive toxicity and hematological effects. Therefore, margins of exposure are derived between lowest exposure levels associated with induction of these effects and conservative estimates of population exposure to DEGME.

The principal routes of exposure to DEGME are expected to be through inhalation and dermal contact during the use of consumer products containing the substance. The maximum concentration measured in indoor air that is considered appropriate for use as a basis for characterizing risk was 39 µg/m³, based on monitoring data collected in Germany between 1989 and 1999 (Schleibinger et al. 2001). Modelling-based estimates of inhalation exposure during use of consumer products containing DEGME are much higher than this (up to 588 mg/m³ for paint remover or stripper). In experimental animal studies, no effects were observed in rats exposed to the highest concentration tested, 1060 mg/m³, for 90 days (Miller et al. 1985), and no mortality was observed in rats exposed to 200 000 mg/m³ for 1 hour or to a saturated atmosphere of DEGME for up to 8 hours (BASF AG 1960; MB Research Laboratories Inc. 1977c). A comparison between the concentration at which no effects were observed in a subchronic study, 1060 mg/m³, and

the measured indoor air concentration of 39 $\mu\text{g}/\text{m}^3$ results in a large margin of exposure of about 27 000. Although using some consumer products containing DEGME could result in peak levels of exposure to airborne DEGME within short time periods, in light of the lack of an inhalation study for developmental toxicity, which appears to be the most sensitive effect, data are considered inadequate for characterizing risk to health associated with exposure to DEGME via inhalation while using products containing this substance.

Dermal contact also contributes significantly to exposure to DEGME during use of some consumer products. Comparison of the highest estimate of exposure to the substance in non-cosmetic products used frequently (0.19 mg/kg-bw per day from use of floor cleaners twice a week) with a “marginal” dermal LOEL of 40 mg/kg-bw per day (EURAR 2000) for minimal effects observed in a 13-week study in guinea pigs (Hobson et al. 1986) results in a margin of exposure of about 210. For floor cleaners, less frequent use would result in lower chronic daily exposure. If the effect level for developmental toxicity is considered (i.e., LO(A)EL of 250 mg/kg-bw per day in a short-term study in rabbits; Scortichini et al. 1986) and compared with the acute per event exposure (0.68 mg/kg-bw per event), the margin of exposure for use of floor cleaners would be 370. For some other types of products used less frequently, the margins between the upper-bounding estimates of exposure to DEGME and the LO(A)EL of 250 mg/kg-bw per day for developmental effects from short-term studies would be smaller; for example, the margin between the estimated exposure of 11 mg/kg-bw per event for use of floor sealer and the LO(A)EL of 250 mg/kg-bw per day is approximately 23. For cosmetic products, based upon available data, modelled exposure estimates for use of multiple products containing the substance could reach 0.27 mg/kg bw per day (Appendix 2). Comparison of this exposure with the “marginal” LOEL of 40 mg/kg-bw per day or the LO(A)EL of 250 mg/kg-bw per day for developmental toxicity results in margins of exposure of approximately 150 or 925, respectively. In summary, the margins for dermal exposure during use of various consumer products (i.e., floor cleaners, floor sealer, latex wall paint, paint remover or stripper, caulking/sealant, floor polish and cosmetic products) may not be adequately protective of human health in light of the uncertainties in the exposure and hazard databases and the serious nature of the health effects associated with exposure to this substance (i.e., developmental toxicity).

With respect to oral exposure to DEGME, levels in drinking water and food are expected to be very low, based on available information on its properties as well as its uses and releases. Margins between predicted oral intakes in drinking water and the critical effect level in studies in orally exposed experimental animals would be very large (i.e., more than 5 orders of magnitude). Therefore, potential oral exposure to DEGME from environmental media in Canada is not expected to be of concern.

Uncertainties in Evaluation of Risk to Human Health

There is some uncertainty regarding quantification of population exposure to DEGME in the general environment, although it is expected that concentrations in environmental media are likely to be low in comparison with exposures associated with the use of consumer products. Only two German studies were identified on concentrations in indoor

air, which may not reflect the Canadian situation. Estimates of exposure from the most frequently used consumer products containing DEGME were based on conservative assumptions and may overestimate actual exposure. However, there is uncertainty with some of the parameters used for the paint and floor cleaner scenarios, such as whether DEGME is actually found in consumer products at the levels presented and the frequency of use in Canada. In addition, there is also some uncertainty associated with the potential exposures from the use of multiple products containing DEGME within a short period of time. Furthermore, there is uncertainty regarding the possible presence of DEGME in fragrances and other personal care products in which it is used as a viscosity decreasing agent and solvent, and actual exposure from use of such products may be significantly greater than that presented in Appendix 2. There is some uncertainty regarding the differences in sensitivity between experimental animals and humans in view of the paucity of epidemiological data, although the critical effects observed in laboratory studies are considered likely relevant to humans, as they are consistent with those reported for other glycol ethers. In addition, there is uncertainty with respect to the carcinogenicity of DEGME due to the lack of long-term studies, although the available information from genotoxicity tests and data on other glycol ethers do not give cause for concern. As well, there is some uncertainty with regard to the potential of DEGME to induce effects via inhalation, particularly developmental effects.

Conclusion

Based on the information presented in this screening assessment, it is concluded that DEGME is not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

Based upon the potential inadequacy of the margins of exposure between conservative estimates of exposure to DEGME during use of consumer products via dermal contact and critical effect levels, particularly for developmental toxicity, in experimental animals, it is concluded that DEGME should be considered as a substance that is entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is therefore concluded that DEGME does not meet the criteria in paragraph 64(a) or 64(b) of CEPA 1999, but it does meet the criteria in paragraph 64(c) of CEPA 1999. Additionally, DEGME does not meet the criteria for persistence or bioaccumulation potential as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

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Appendix 1. Upper bounding estimates of daily intake of DEGME by the general population in Canada

Route of exposure	Estimated intake ($\mu\text{g}/\text{kg}\text{-bw}$ per day) of DEGME by various age groups						
	0–6 months ^{1, 2, 3}		0.5–4 years ⁴	5–11 years ⁵	12–19 years ⁶	20–59 years ⁷	60+ years ⁸
	Formula fed	Not formula fed					
Ambient air ⁹	<0.001		<0.001	<0.001	<0.001	<0.001	<0.001
Indoor air ¹⁰	9.6		20.5	16.0	9.1	7.8	6.8
Drinking water ¹¹	0.004	0.001	0.002	0.001	<0.001	<0.001	<0.001
Food and beverages ¹²	NA	NA	NA	NA	NA	NA	NA
Soil ¹³	<0.001		<0.001	<0.001	<0.001	<0.001	<0.001
Total intake	9.6	9.6	20.5	16.0	9.1	7.8	6.8

NA, not available.

¹ No data were identified on concentrations of DEGME in breast milk.

² Assumed to weigh 7.5 kg, to breathe 2.1 m³ of air per day, to drink 0.8 L of water per day (formula fed) or 0.3 L/day (not formula fed) and to ingest 30 mg of soil per day (Health Canada 1998).

³ For exclusively formula-fed infants, intake from water is synonymous with intake from food. The concentration of DEGME in water used to reconstitute formula was based on modelling. No data on concentrations of DEGME in formula were identified for Canada or elsewhere. Approximately 50% of non-formula-fed infants are introduced to solid foods by 4 months of age and 90% by 6 months of age (NHW 1990).

⁴ Assumed to weigh 15.5 kg, to breathe 9.3 m³ of air per day, to drink 0.7 L of water per day and to ingest 100 mg of soil per day (Health Canada 1998).

⁵ Assumed to weigh 31.0 kg, to breathe 14.5 m³ of air per day, to drink 1.1 L of water per day and to ingest 65 mg of soil per day (Health Canada 1998).

⁶ Assumed to weigh 59.4 kg, to breathe 15.8 m³ of air per day, to drink 1.2 L of water per day and to ingest 30 mg of soil per day (Health Canada 1998).

⁷ Assumed to weigh 70.9 kg, to breathe 16.2 m³ of air per day, to drink 1.5 L of water per day and to ingest 30 mg of soil per day (Health Canada 1998).

⁸ Assumed to weigh 72.0 kg, to breathe 14.3 m³ of air per day, to drink 1.6 L of water per day and to ingest 30 mg of soil per day (Health Canada 1998).

⁹ No measured data were identified. Modelling using ChemCAN 6.0 (ChemCAN 2003) and selecting Average for Canada region indicated that the concentration of DEGME in ambient air would be approximately 1.8×10^{-5} $\mu\text{g}/\text{m}^3$, based on the upper-end range of DEGME (100 000 kg) released to air, derived from information submitted by industry (Environment Canada 2008a).

¹⁰ No Canadian-specific data on concentrations of DEGME in indoor air were identified. The maximum concentration identified in the literature was 39 $\mu\text{g}/\text{m}^3$, from a study conducted in Berlin, Germany, between 1989 and 1999 (Schleibinger et al. 2001). Canadians are assumed to spend 21 hours indoors each day (Health Canada 1998). One other study was identified, but the maximum concentration (164 $\mu\text{g}/\text{m}^3$) was much higher than the 95th-percentile value (0.4 $\mu\text{g}/\text{m}^3$) and was therefore not considered to represent a typical concentration in indoor air (Plieninger and Marchl 1999).

¹¹ No measured data were identified. Modelling using ChemCAN 6.0 (ChemCAN 2003) and selecting Average for Canada region indicated that the concentration of DEGME in water would be approximately 0.034 $\mu\text{g}/\text{L}$, based on the upper-end range of DEGME (100 000 kg) released to water, derived from information submitted by industry (Environment Canada 2008a).

¹² No measured data were identified.

¹³ No measured data were identified. Modelling using ChemCAN 6.0 (ChemCAN 2003) and selecting Average for Canada region indicated that the concentration of DEGME in soil would be approximately 9.2×10^{-4} $\mu\text{g}/\text{kg}$, based on the maximum estimated quantity of DEGME (0.1 kg) released during formulation, processing and use and specific information on releases to land submitted by industry (Environment Canada 2008a).

Appendix 2. Upper bounding estimates of exposure to DEGME in consumer products, based on ConsExpo version 4.1 (ConsExpo 2006)

Consumer product scenarios	Assumptions ¹	Estimated exposure
Latex wall paint (brush/roller painting, waterborne wall paint)	<p>Maximum reported weight fraction of 5% (HPD 2008; Sherwin-Williams 2008)</p> <p>Inhalation: Evaporation from increasing area Exposure duration of 132 min, application duration of 120 min, product amount of 3750 g, room volume of 20 m³, ventilation rate of 0.6/h, release area of 15 m², temperature of 20°C, use Thibodeaux method for mass transfer rate, molecular weight matrix of 120 g/mol (RIVM 2007a)</p> <p>Dermal: Constant rate Contact rate of 30 mg/min, release duration of 120 min (RIVM 2007a)</p>	<p>Inhalation – Mean event concentration 42 mg/m³</p> <p>Dermal – Acute applied dose 2.5 mg/kg-bw per event</p>
Paint remover	<p>Maximum reported weight fraction of 7.9% (Environment Canada 2008a)</p> <p>Inhalation: Evaporation from increasing area Exposure and application duration of 60 min, product amount of 1 kg, room volume of 20 m³, ventilation rate of 0.6/h, release area of 2 m², temperature of 20°C, use Langmuir method for mass transfer rate, molecular weight matrix of 3000 g/mol (RIVM 2007b)</p> <p>Dermal: Instant application Exposed surface area of 430 cm², applied amount of 0.5 g (RIVM 2007b)</p>	<p>Inhalation – Mean event concentration 588 mg/m³</p> <p>Dermal – Acute applied dose 0.56 mg/kg-bw per event</p>
Brake fluid	<p>Maximum reported weight fraction (WF) of 2% (Environment Canada 2008a)</p> <p>Inhalation: No ConsExpo scenario. Assume done outdoors or in well-ventilated area.</p> <p>Dermal: No ConsExpo scenario. The standard scenario in US EPA (1986) describes a typical exposure to brake fluid while bleeding the brake lines of an automobile. The process involves opening a valve on the brake line while someone pumps the brake pedal. Dermal exposure can occur as a result of deposition of brake fluid onto skin while opening and closing the valve on the brake line.</p> <p>Thin-film thickness estimation with the following default values: film thickness (FT) of 15.88×10^{-3} cm, density of product (D) of 0.85 g/cm³ (US EPA 1986), exposed surface area (SA)² of 15 cm²</p> <p>Estimated dose $= \frac{SA \times FT \times D \times WF}{BW}$ $= (15 \text{ cm}^2) (0.015 \text{ 88 cm}) (0.85 \text{ g/cm}^3) (0.02) / 70.9 \text{ kg}$ $= 5.7 \times 10^{-5} \text{ g/kg-bw per day or } 0.057 \text{ mg/kg-bw per day}$</p>	<p>Dermal – Acute applied dose 0.057 mg/kg-bw per event</p>
Caulking/sealant (joint)	Maximum reported weight fraction of 5% (GE 2003)	Inhalation – Mean event concentration

Consumer product scenarios	Assumptions ¹	Estimated exposure
sealant)	<p>Inhalation: Evaporation from increasing area Exposure duration of 45 min, application duration of 30 min, product amount of 75 g, room volume of 10 m³, ventilation rate of 2/h, release area of 250 m², temperature of 20°C, use Langmuir method for mass transfer rate, molecular weight matrix of 3000 g/mol (RIVM 2007b)</p> <p>Dermal: Constant rate Exposed area of 2 cm², contact rate of 50 mg/min, release duration of 30 min (RIVM 2007b)</p>	<p>135 mg/m³</p> <p>Dermal – Acute applied dose 1.1 mg/kg-bw per event</p>
Floor sealer (floor seal products)	<p>Maximum reported weight fraction of 5% (ZEP 2007; HPD 2008)</p> <p>Inhalation: Evaporation from increasing area Exposure and application duration of 90 min, product amount of 1500 g, room volume of 58 m³ (living room), ventilation rate of 0.5/h, release area of 22 m², temperature of 20°C, use Langmuir method for mass transfer rate, molecular weight matrix of 22 g/mol (RIVM 2006b)</p> <p>Dermal: Instant application Exposed area of 430 cm², applied amount of 15 g (1% of 1500 g) (RIVM 2006b)</p>	<p>Inhalation – Mean event concentration 11 mg/m³</p> <p>Dermal – Acute applied dose 10.6 mg/kg-bw per event</p>
Floor polish	<p>Maximum reported weight fraction of 6% (Reckitt Benckiser 2004; HPD 2008)</p> <p>Inhalation: Evaporation from increasing area Exposure and application duration of 90 min, product amount of 550 g, room volume of 58 m³ (living room), ventilation rate of 0.5/h, release area of 22 m², temperature of 20°C, use Langmuir method for mass transfer rate, molecular weight matrix of 22 g/mol (RIVM 2006b)</p> <p>Dermal: Instant application Exposed area of 430 cm², product amount of 5.5 g (1% of 550 g) (RIVM 2006b)</p>	<p>Inhalation – Mean event concentration 12 mg/m³</p> <p>Dermal – Acute applied dose 4.7 mg/kg-bw per event</p>
Floor cleaner – mixing and loading (floor cleaning liquids: mixing and loading)	<p>Maximum reported weight fraction of 5% (Reckitt Benckiser 2005; HPD 2008)</p> <p>Inhalation: Evaporation from constant surface Exposure duration of 0.75 min, application duration of 0.3 min, product amount of 500 g, breathing zone (personal volume) of 1 m³, ventilation rate of 0.5/h, release area of 0.002 m², temperature of 20°C, use Langmuir method for mass transfer rate, molecular weight matrix of 22 g/mol (RIVM 2006b)</p> <p>Dermal: Instant application Exposed area of 215 cm², product amount of 0.010 g, frequency of 104/year (RIVM 2006b)</p>	<p>Inhalation – Mean event concentration 8.5 mg/m³</p> <p>Dermal – Acute applied dose 0.0071 mg/kg-bw per event</p> <p>Dermal – Chronic applied dose 0.0020 mg/kg-bw per day</p>
Floor cleaner – application (floor cleaning liquid: cleaning)	<p>Maximum reported weight fraction of 5% (Reckitt Benckiser 2005; HPD 2008), diluted by a factor of 20 (weight fraction = 0.0025) (RIVM 2006b)</p> <p>Inhalation: Evaporation from increasing area</p>	<p>Inhalation – Mean event concentration 0.43 mg/m³</p> <p>Dermal – Acute</p>

Consumer product scenarios	Assumptions ¹	Estimated exposure
	<p>Exposure duration of 240 min, application duration of 30 min, product amount of 880 g (diluted), room volume of 58 m³ (living room), ventilation rate of 0.5/h, release area of 22 m², temperature of 20°C, use Langmuir method for mass transfer rate, molecular weight matrix of 18 g/mol (RIVM 2006b)</p> <p>Dermal: Instant application Exposed area of 1900 cm², product amount of 19 g (diluted), frequency of 104×/year (RIVM 2006a, b)</p>	<p>applied dose 0.67 mg/kg-bw per event</p> <p>Dermal – Chronic applied dose 0.19 mg/kg-bw per day</p>
Floor cleaner – combined scenario (mixing, loading and application)	<p>Combined scenario Because these two scenarios would likely occur on the same day, the event concentrations and applied doses for the two scenarios have been combined.</p>	<p>Inhalation – Mean event concentration 8.9 mg/m³</p> <p>Dermal – Acute applied dose 0.68 mg/kg-bw per event</p> <p>Dermal – Chronic applied dose 0.19 mg/kg-bw per day</p>
Body cream ³	<p>Dermal: Instant application Maximum reported weight fraction of 0.1% (CNS 2008), surface area of 16 925 cm² (area of body – half area of head) (Health Canada 1995), frequency of 730×/year or 2×/day, amount of product of 8 g (RIVM 2006a), assume a retention factor of 1</p>	<p>Dermal – Chronic applied dose 0.23 mg/kg-bw per day</p>
Face cream ³	<p>Dermal: Instant application Maximum reported weight fraction of 0.1% (CNS 2008), surface area of 638 cm² (half area of head) (Health Canada 1995), frequency of 730×/year or 2×/day, amount of product of 0.8 g (RIVM 2006a), assume a retention factor of 1</p>	<p>Dermal – Chronic applied dose 0.023 mg/kg-bw per day</p>
Facial cleanser ³	<p>Dermal: Instant application Maximum reported weight fraction of 0.1% (CNS 2008), surface area of 638 cm² (half area of head) (Health Canada 1995), frequency of 730×/year or 2×/day, amount of product of 2.5 g (RIVM 2006a), assume a retention factor of 0.1</p>	<p>Dermal – Chronic applied dose 0.0071 mg/kg-bw per day</p>
Hairspray	<p>Maximum reported weight fraction of 0.1% (CNS 2008)</p> <p>Inhalation: Exposure to spray – spraying towards exposed person Spray duration of 0.24 min, exposure duration of 5 min, room volume of 10 m³ (bathroom), room height of 2.5 m, ventilation rate of 2/h, cloud volume of 0.0625 m³, mass generation rate of 0.47 g/s, airborne fraction 1 g/g, weight fraction non-volatile of 0.03 g/g, density non-volatile of 1.5 g/cm³, initial particle distribution median (coefficient of variation) of 35 µm (0.3), inhalation cut-off diameter of 15 µm (RIVM 2006a)</p> <p>Dermal: Instant application Exposed area of 638 cm² (half area of head) (Health Canada 1995), product amount upon head of 0.6 g, frequency of 438×/year (RIVM 2006a), assume a retention factor of 1</p>	<p>Inhalation – Mean event concentration 0.0014 mg/m³</p> <p>Dermal – Chronic applied dose 0.01 mg/kg-bw per day</p>

Consumer product scenarios	Assumptions¹	Estimated exposure
Total exposure to personal care products	Because body and face cream, facial cleanser and hairspray could all be used in the same day, the dermal exposure values are combined.	Dermal – Chronic applied dose 0.27 mg/kg-bw per day

¹ The following assumptions were applied to all scenarios: body weight: 70.9 kg for an adult and inhalation rate of 16.2 m³/day (Health Canada 1998).

² Exposed surface area was assumed for fingertips while working with brake lines. Each fingertip has an area of 1.5 cm² (1 cm × 1.5 cm), and therefore the total fingertip area is 15 cm².

³ Inhalation: not considered for this scenario (RIVM 2006a).

Appendix 3. Summary of health effects information for DEGME

Endpoint	Lowest effect levels ¹ /Results
Laboratory animals and <i>in vitro</i>	
Acute toxicity	<p>Lowest oral LD₅₀ (guinea pig) = 4160 mg/kg-bw (Smyth et al. 1941) [additional studies: Smyth et al. 1941; MB Research Laboratories Inc. 1977a; Krasavage and Terhaar 1981; Union Carbide Corporation 1984]</p> <p>Lowest dermal LD₅₀ (rabbit) = 6540 mg/kg-bw (Union Carbide Corporation 1967) [additional studies: Browning 1965; MB Research Laboratories Inc. 1977b; Krasavage and Terhaar 1981]</p> <p>Lowest inhalation LC₅₀ (rat, 1 h) = >200 mg/L (no mortality (0/10), no clinical toxicity was observed, 3 animals had dark staining of liver and kidneys), equivalent to 200 000 mg/m³ (MB Research Laboratories Inc. 1977c) [additional inhalation studies: BASF AG 1960; Union Carbide Corporation 1984]</p>
Short-term repeated-dose toxicity	<p>Lowest oral LO(A)EL = 1000 mg/kg-bw per day (Wistar rats, 4–8 males/group, gavage for 20 days), based on significantly reduced relative thymus weights. Absolute organ weight changes were not reported. At a higher dose level (2000 mg/kg-bw per day), significantly reduced relative testes weights and severe lymphocyte depletion in the thymus cortex were observed. NOEL = 500 mg/kg-bw per day (Kawamoto et al. 1990).</p> <p>[additional studies: effects on body weights and organ weights, including thymus, testes, liver, kidney, spleen, brain, heart and pituitary gland, and altered hematological parameters were observed (Smyth and Carpenter 1948²; Krasavage and Vlaovic 1982; Nagano et al. 1984; Schuler et al. 1984; Hardin et al. 1986; Kawamoto and Kodama 1989; Kawamoto et al. 1990, 1991, 1992; Smialowicz et al. 1992; Yamano et al. 1993)]</p> <p>Lowest dermal LO(A)EL = 750 mg/kg-bw per day (pregnant rabbits, 25/group, through gestation days 6–18), based on maternal toxicity effects, including significantly reduced red blood cell counts and packed cell volume and reduced body weight gain. The dermal NO(A)EL = 250 mg/kg-bw per day (Dow Chemical 1983a, b; Scortichini et al. 1986).</p>

Endpoint	Lowest effect levels ¹ /Results
Subchronic toxicity	<p>No exposure-related effects were observed in rats administered 1% DEGME in drinking water (1400 mg/kg-bw per day, 4 rats/group) for 110 days. These 4 rats and an additional 5 rats were subsequently administered 3–5% DEGME in drinking water (4200–7000 mg/kg-bw per day) for 11–64 days. One rat died at 64 days. Kidney damage was observed in 3 rats killed at 28 days (2 rats) and 45 days (1 rat). Drinking water consumption was reduced (no further details) (Kesten et al. 1939). [no additional oral studies identified]</p> <p>The European Commission (EURAR 2000) established a “marginal” dermal effect level (lowest dermal LOEL) = 40 mg/kg-bw per day (guinea pig, 6/dose, dermal exposure 6 h/day, 5 days/week, for 13 weeks), based on slight histopathological changes in the liver and elevated urinary calcium level. At higher dose levels (≥ 200 mg/kg-bw per day), significantly increased serum lactate dehydrogenase and mean corpuscular hemoglobin concentrations, significantly decreased spleen weights and significantly increased hepatocellular fatty changes were observed (Hobson et al. 1986).</p> <p>Inhalation NO(A)EC = ≥ 216 ppm, equivalent to 1060 mg/m³ (the highest concentration tested) (F344 rats, 10/sex per group, 6 h/day, 5 days/week, for 90 days). No exposure-related effects on body weights, organ weights, hematological analyses, clinical chemistry analyses, urinalyses, and gross and histopathological examinations were observed (Miller et al. 1985).</p>
Chronic toxicity/ carcinogenicity	No data identified
Reproductive toxicity	<p>Lowest oral LO(A)EL = 2000 mg/kg-bw per day (Wistar rats, 4–8 males/group, gavage for 20 days), based on significantly decreased relative testis weights. Absolute organ weight changes were not reported. The oral NO(A)EL = 1000 mg/kg-bw per day (Kawamoto et al. 1990).</p> <p>Although significantly increased relative testes weights were observed at 1800 mg/kg-bw per day (albino rats, 10 males/group, gavage, 6 weeks), absolute testes weights did not change at this dose level. It is possible that the relative testes weight changes were the consequence of the significantly reduced rat body weights. At a higher dose level (3600 mg/kg-bw per day), significantly reduced absolute and relative testes weights, due to the testicular atrophy, along with degenerated spermatozoa and/or hypospermia in the epididymis were observed. The oral NO(A)EL = 900 mg/kg-bw per day (Krasavage and Vlaovic 1982).</p> <p>[additional studies: Nagano et al. 1984 (2% DEGME was administered to male mice, 4/group, in drinking water, equivalent to 4000 mg/kg-bw per day, for 25 days. Slightly decreased testicular weights were observed, which did not reach statistical significance)]</p>

Endpoint	Lowest effect levels ¹ /Results
Developmental toxicity	<p>Lowest oral LO(A)EL = 600 mg/kg-bw per day (pregnant Wistar rats, 22/group, gavage through gestation days 7–17), based on significantly decreased fetal body weights in both sexes, significantly increased incidence of visceral variations such as unilateral or bilateral thymic remnants in the neck, and significantly impaired ossification in sternbrae and in thoracic, sacral and caudal vertebrae. At a higher dose level (1800 mg/kg-bw per day), more severe teratogenic and developmental toxic effects were observed, including significantly increased fetal resorption and prolonged duration of gestation; significantly increased incidence of fetal visceral malformations in the cardiovascular system, higher incidence of variations in thymus and kidneys, and fetal external malformations, such as anasarca and anury, and fetal skeletal variations in ribs and in thoracic and lumbar vertebrae; significantly increased incidence of dilated renal pelvis; significantly delayed fetal ossification in sternbrae, limbs and vertebrae; significantly decreased postnatal viability of offspring. Maternal toxicity was also observed, including significantly reduced body weight gain, food consumption and thymus weights. The oral NO(A)EL = 200 mg/kg-bw per day (Yamano et al. 1993).</p> <p>[additional oral studies: Hardin et al. 1986 (pregnant Sprague-Dawley rats administered DEGME in drinking water on gestation days 7–16, LO(A)EL = 720 mg/kg-bw per day, primarily based on fetal visceral and skeletal malformations); Schuler et al. 1984 (Chernoff/Kavlock test in pregnant CD-1 mice administered 4000 mg DEGME/kg-bw per day via gavage on gestation days 7–14; significantly reduced viable litter index, reduced number of live pups per litter and reduced pup survival over days 1–3 postpartum were observed)]</p> <p>Lowest dermal LO(A)EL = 250 mg/kg-bw per day (pregnant rabbits, 25/group, through gestation days 6–18), based on significantly delayed ossification in the fetal skull and cervical spur vertebrae. At higher dose levels, a significantly increased incidence of fetal alterations, including mild forelimb flexure, dilated renal pelvis and retrocaval ureter, delayed sternbrae ossification and increased fetal resorptions were observed. Maternal toxicity, including significantly decreased body weight gain and reduced red blood cell counts and packed cell volume, was observed only at the highest dose level (750 mg/kg-bw per day). The dermal NO(A)EL = 50 mg/kg-bw per day (Scortichini et al. 1986). [additional dermal study: Dow Chemical 1983a, b (range-finding studies (100–1000 mg/kg-bw per day) for the above-described teratogenicity test in rabbits)]</p> <p>No inhalation data identified</p>
Genotoxicity and related endpoints: <i>in vivo</i>	No data identified
Genotoxicity and related endpoints: <i>in vitro</i>	<p>Mutagenicity Negative: Ames tests in <i>Salmonella typhimurium</i> TA98, TA100, TA1535, TA1537, TA1538, with and without metabolic activation (ICI 1980; BASF AG 1989)</p> <p>Chromosomal aberration Negative: Chinese hamster V79 cells with and without activation (Müller 1997)</p>
Immunotoxicity	DEGME did not suppress the primary plaque-forming cell response to trinitrophenyl-lipopolysaccharide in male F344 rats (6/group) orally administered DEGME by gavage at 100–800 mg/kg-bw per day (Smialowicz et al. 1992). However, T-cell depletion was observed in the thymus of orally administered male Wistar rats (Kawamoto et al. 1990).

Endpoint	Lowest effect levels ¹ /Results
Sensitization	DEGME is not a skin sensitizer when tested in guinea pigs and humans (Kligman 1972; Pastushenko et al. 1985; Bury 1997).
Irritation	Skin irritation DEGME is not irritating to skin in several studies conducted in rabbits (Dow Chemical 1954; BASF AG 1960; MB Research Laboratories Inc. 1977b; Union Carbide Corporation 1984).
	Eye irritation DEGME is not irritating to eye in a study in rabbits (Union Carbide Corporation 1984). Other studies showed that DEGME is slightly irritating to eye in rabbits (Carpenter and Smyth 1946; MB Research Laboratories Inc. 1977d).
Human	Case report: A 5 year old boy was diagnosed with retrocaval ureter as well as cardiovascular and skeletal anomalies. His mother had worked in a local weaving company in the thread-dyeing section with direct exposure to dyes during the previous 7 years. The authors speculated that one of the etiologic factors for the boy's developmental effects may have been maternal contact with DEGME or ethylene glycol monomethyl ether (Karaman et al. 2002).

¹ LC₅₀, median lethal concentration; LD₅₀, median lethal dose; LO(A)EL, lowest-observed-(adverse-)effect level; LOEL, lowest-observed-effect level; NO(A)EC, no-observed-(adverse-)effect concentration; NO(A)EL, no-observed-(adverse-)effect level.

² This is a dose-finding study; some unspecified micropathological changes in liver, kidney, spleen and testes were observed in rats at ≥ 190 mg/kg-bw per day dose levels administered in drinking water. However, the European Commission deemed that this study was not relevant for the derivation of an overall NO(A)EL due to the range-finding character of this study and the fact that only the summarized data were available (EURAR 2000).