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METHYLOXIRANE
(PROPYLENE OXIDE)

CAS No: 75-56-9

EINECS No: 200-879-2

Summary Risk Assessment Report

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SUMMARY RISK ASSESSMENT REPORT

Final report, 2002

United Kingdom

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PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance methyloxirane that has been prepared by the United Kingdom in the context of Council Regulation (EEC) No. 793/93 on the evaluation and control of existing substances.

For detailed information on the risk assessment principles and procedures followed, the underlying data and the literature references the reader is referred to the original risk assessment report that can be obtained from the European Chemicals Bureau¹. The present summary report should preferably not be used for citation purposes.

¹ European Chemicals Bureau – Existing Chemicals – <http://ecb.jrc.it>

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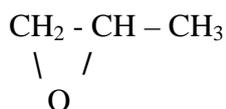
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1

GENERAL SUBSTANCE INFORMATION

Identification of the substance

CAS-No.: 75-56-9
EINECS-No.: 200-879-2
IUPAC name: methyloxirane
Synonyms: propylene oxide, 1,2-epoxypropene, propenoxide
Molecular formula: C₃H₆O
Structural formula:



Molecular weight: 58.08

Physico-chemical properties

Table 1.1 Properties of propylene oxide

Property	Value
Melting point	-112.16°C
Boiling point	33.9 - 34.3°C at 101.3 kPa (34.1°C)
Relative density	0.83
Vapour pressure	58.4 - 61.2 kPa at 20°C (59.8 kPa)
Water solubility	395 - 405 g l ⁻¹ at 20°C (pH=7) (400 g l⁻¹)
Log octanol/water partition coefficient	0.03 - 0.08 (0.055)
Flammability	Flash point: -37 to -44°C (closed cup)
Autoflammability	420 - 430°C
Explosive properties	Lower explosive limit: 1.9 - 2.8% v/v Upper explosive limit: 21.5 - 45% v/v
Vapour density	2.05 (air=1)
Surface tension	23.5 mN m ⁻¹ at 20°C (propylene oxide)
Viscosity	0.28 mPa.s at 25°C
Conversion factor	1 ppm = 2.41 mg m ⁻³ at 25°C

Note: values in bold in parentheses are those used in the environmental exposure assessment

Classification and labelling

Classification and labelling according to the 28th ATP of Directive 67/548/EEC²:

F+; R12	Extremely flammable
Carc. Cat. 2; R45	May cause cancer
Muta. Cat. 2; R46	May cause heritable genetic damage
Xn; R20/21/22	Also harmful by inhalation, in contact with skin and if swallowed
Xi; R36/37/38	Also irritating to eyes, respiratory system and skin
Nota E	
S45	In case of accident or if you feel unwell, seek medical advice immediately (show label where possible)
S53	Avoid exposure - obtain special instructions before use

Additional information – The CMR group concluded that the information on skin sensitisation did not meet the criteria for classification as a sensitiser.

No classification for the environment.

² The classification of the substance is established by Commission Directive 2001/59/EC of 6 August 2001 adapting to the technical progress for the 28th time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances (OJ L 225, 21.8.2001, p.1).

2

GENERAL INFORMATION ON EXPOSURE

There are two main production routes for propylene oxide. The chlorohydrin process involves reaction between propylene and chlorine followed by epoxidation; this accounted for 53% of EU production in 1992. The second method involves indirect oxidation and produces t-butanol or styrene as a co-product depending on the starting material (32% and 15% of EU propylene oxide production respectively). World production was 3,585,000 tonnes in 1990. Annual EU production is estimated to be 1,445,000 tonnes, with an extra 50,000 tonnes imported.

Propylene oxide is used in three areas: as a monomer in polymer production; as an intermediate in the synthesis of other substances; and as a stabiliser for dichloromethane. The last of these accounts for only a small proportion of the tonnage used.

Its use as a monomer or chemical intermediate is for the manufacture of the following:

- polyols used in polyurethane foam manufacture for the furniture and automotive industries, and coatings, adhesives and sealants.
- propylene glycol ethers for use as solvents in paints, inks, coatings, resins, cleaners and waxes.
- propylene glycols, which can be used in:
 1. the production of unsaturated polyester resins, especially in the textile and construction industries;
 2. as a solvent in food, pharmaceuticals and cosmetics;
 3. in engine coolants and aircraft de-icers.
- butanediol and related products for speciality resins and solvents.

Table 2.1 shows the breakdown of use between the major areas.

Table 2.1 Propylene oxide use by product in 1982

Product	EU	United States	Canada
Polyether polyols	72%	64%	65%
Propylene glycols	23%	21%	29%
Other uses	5%	15%	6%

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

Propylene oxide reacts with hydroxyl radicals in the atmosphere with an estimated half-life of 32 days. In water it undergoes hydrolysis, both spontaneously and through acid- or base-catalysis. This process has an estimated half-life of 22 days under environmental conditions.

A range of test data is available for biodegradation. On the basis of the available evidence, it is clear that propylene oxide can be degraded biologically, but that this may not always happen under the conditions required for ready degradability. Therefore the substance is assumed to be inherently degradable in general, but readily biodegradable where the bacterial population has become acclimatised (such conditions will apply where there are continuous releases of propylene oxide to a waste water treatment plant, such as for large production and processing sites).

Propylene oxide has a low log K_{ow} value (0.055), and so is not expected to bioaccumulate or to adsorb strongly to organic matter in sediments and soils.

Releases from production and use

The assessment considers releases from production of propylene oxide, from its use in the production of polymers and other substances and from their subsequent use, from direct use and from possible indirect sources. Specific information from industry was used to estimate releases for production and use in the production of polymers and other substances. Measurements of residual concentrations of propylene oxide in products were used to estimate releases from products in use. Releases from the direct use as a stabiliser in dichloromethane were based on estimates for Germany. Indirect sources such as car exhausts were discussed but not considered significant. The releases estimated are summarised in **Table 3.1**.

Table 3.1 Summary of releases of propylene oxide

Activity	Release (tonnes/year)					
	Local scale		Regional scale		Continental scale	
	Air	Water	Air	Water	Air	Water
Production	5.5	13	55	130	159	376
Processing	8.3	15.7	8.3	15.7	55.3	105
Further processing	0.18 ^{a)}		0.54 ^{a)}	0.54 ^{a)}	5.4 ^{a)}	5.4 ^{a)}
Direct use			5		50	
Total			68.8	146	270	486

^{a)} Based on estimates from polyurethane production; larger scale estimates use this value for all further processing of propylene oxide, and assign all release to air and to water (i.e. these releases are double counted)

Predicted environmental concentrations (PECs)

There are very few measured concentrations of propylene oxide in the environment. The assessment is therefore based on calculated concentrations. Site-specific concentrations in air and water were calculated for most of the production and processing sites. These cover 97% of the production tonnage and 60% of the processing tonnage, and are taken to be representative of these steps in the life cycle. Concentrations in air were calculated for the further processing of materials containing residual propylene oxide. The methods from the Technical Guidance Document (TGD) were used to derive concentrations in sediment and soil, and the EUSES programme used to calculate concentrations on the regional scale. The results of these calculations are summarised in **Table 3.2**.

Table 3.2 Summary of PECs for propylene oxide

	Water ($\mu\text{g/l}$)	Sediment ($\mu\text{g/kg}$)	Air ($\mu\text{g/m}^3$)	Soil ($\mu\text{g/kg}$) ^{b)}
Production / processing ^{a)}	2.0	1.9	17	3.3
Further processing	-	-	0.15	0.026
Regional	$6.7 \cdot 10^{-4}$	0.055	$5.4 \cdot 10^{-3}$	$4.1 \cdot 10^{-4}$

a) Many sites combine production and processing; the table takes the highest concentration from the specific site results for each compartment. Hence the values for the various compartments do not necessarily come from the same site

b) For soil the assessment considers grassland and arable land, and the values here are the higher of the two - in fact the values were very similar between the soil types

3.2 EFFECTS ASSESSMENT

Surface water

Short-term toxicity data are available for fish, invertebrates and algae. The data selected for use in the assessment (the lowest valid result for each organism) are in **Table 3.3**.

Table 3.3 Aquatic toxicity of propylene oxide

Organism	Endpoint	Concentration (mg/l)
Rainbow trout <i>Oncorhynchus mykiss</i> (fish)	96-hour LC ₅₀	52
Daphnia magna (invertebrate)	48-hour EC ₅₀	350
Selenastrum capricornutum (alga)	96-hour EC ₅₀	240

As only acute data are available, an assessment factor of 1,000 is applied to the lowest result from the table, giving a predicted no-effect concentration for the aquatic compartment (PNEC_{water}) of 52 $\mu\text{g/l}$.

Sediment

There are no data on effects on sediment dwelling organisms, and so the equilibrium partitioning method was used, giving a PNEC_{sed} of 43 $\mu\text{g/kg}$.

Wastewater treatment plant

For microorganisms, there are no specific toxicity test results, but ready biodegradation was observed in a test at 100 mg/l, and there is evidence of high levels of removal from wastewater treatment plants.

Terrestrial compartment

Propylene oxide has been tested as a fumigant in soil, but at very high levels compared to those expected in the environment. Therefore the equilibrium partitioning method was used to derive the PNEC_{soil} of 16.5 µg/kg.

Atmosphere

Propylene oxide degrades in air but only at a moderate rate, and so is not thought likely to contribute to low-level ozone formation.

Secondary poisoning

In view of the properties of the substance a secondary poisoning assessment has not been carried out.

3.3 RISK CHARACTERISATION

The risk characterisation is performed by comparing the PEC with the relevant PNEC for each environmental compartment / endpoint (no comparison is possible for wastewater treatment plant or air). A ratio above 1 indicates a concern. The resulting ratios are in **Table 3.4**.

Table 3.4 PEC/PNEC ratios for propylene oxide

	Water	Sediment	Soil
Production / processing	0.04	0.04	0.2
Further processing	-	-	0.002
Regional	0.001	0.001	2.4 · 10 ⁻⁵

There is therefore currently no concern for the environment.

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

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

Occupational exposure

Occupational exposure to propylene oxide occurs during its manufacture and use as a chemical intermediate. It is therefore always used in closed plant with exposures arising during tasks where the system is breached, such as sampling, tanker filling and emptying, and unplanned and periodic maintenance. This industry employs and develops measures to reduce exposure to as low a level as reasonably practicable, such as the use of enclosed sampling points and dry break coupling systems for tanker filling and emptying. Industry data indicate that exposure can be controlled to less than 3 ppm 8-hour TWA, with the majority of exposures less than 1 ppm 8-hour TWA. Short-term exposures of between 0.06 and 41.7 ppm have been reported during uncoupling. Modelled exposures were 33 to 67 ppm 15-minute TWA for uncoupling and greater than 33 ppm 15-minute TWA for sampling.

Dermal exposure can occur during the production and use of propylene oxide, where operators come into contact with surfaces contaminated from splashing or condensed vapour, or as a result of direct contact onto the skin. As processing is in closed systems, dermal exposure is only likely during activities such as sampling and the uncoupling of pipes. The contribution from condensed vapour is likely to be minimal due to its volatility. EASE predicted this to be 0 to 0.1 mg/cm²/day. Exposure will be towards the bottom of this range, although the upper end of the range may reflect exposure during maintenance activities where dermal contact is greater. Similar dermal exposures were predicted for laboratory technicians handling propylene oxide during electron microscopy work. For operators using dichloromethane stabilised with propylene oxide, dermal exposures were predicted to be 0.005 to 0.025 mg/cm²/day. Operators are likely to wear gloves where the potential for skin contact exists and thus further reduce these predicted exposures.

Consumer exposure

Propylene oxide has no direct consumer use as a monomer. Intermediates derived from propylene oxide may be used in products for consumer use, and may contain residual amounts of the monomer. The intermediates derived from propylene oxide are mainly glycols, glycol ethers and polyether polyols. These have a variety of applications including consumer applications such as hydraulic fluids (brake fluid for cars), foodstuffs and medicinal products. However, the amount of residual monomer present in final products used by consumers is very low and therefore consumer exposure is expected to be negligible.

Humans exposed via the environment

Exposure via the environment is estimated to be 3.9 µg/kg/day for the local scenario and 3 ng/kg/day for the regional scenario.

Combined exposure

A worst-case combined exposure scenario is composed of exposure in the workplace and to the highest local environmental exposure levels. No quantitative estimate of total exposure from inhalation, dermal and oral routes, is possible. As described above, exposure in the workplace will be kept to a minimum due to the controls in place to minimise exposure to isocyanates. Exposure via the environment is also very low.

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

Propylene oxide and/or its metabolites are readily absorbed through the gastrointestinal and respiratory tracts and widely distributed to the major organs. No data are available for dermal absorption but acute toxicity data indicate the potential for dermal absorption of the liquid. No conclusions can be drawn regarding the potential for dermal absorption of the vapour. Metabolism involves conjugation with glutathione or hydrolysis by epoxide hydrolase. Excretion of propylene oxide and its metabolites is expected to be primarily via urine and expired air. Propylene oxide binds to, or reacts with, tissue proteins and nucleic acids *in vitro* and *in vivo*. Haemoglobin adducts have been quantified in animals and humans exposed to propylene oxide. DNA binding as assessed by adduct formation has been observed in several animal tissues following inhalation exposure.

In studies in rodents, propylene oxide is harmful following inhalation, oral and dermal exposure. Liquid propylene oxide is irritating to the skin, and is probably irritating to the eyes and respiratory tract. Propylene oxide vapour has caused irritation of the eyes and upper respiratory tract (but not the skin) in humans.

There is limited human evidence that propylene oxide may cause skin sensitisation. There are no conventional skin sensitisation studies in animals. In the only available study, the result was negative. Overall, this substance has not been adequately tested for skin sensitisation and consequently the risk assessment does not evaluate the risks to any human population for this endpoint. There are no reports of propylene oxide causing respiratory sensitisation and it is not possible to draw any conclusions regarding this end-point.

In rats and mice, repeated inhalation exposure for two years produces chronic irritation of the nasal epithelium; at 30 ppm such effects are marginal in nature, whereas concentrations of 100 ppm and above produce pronounced nasal epithelial damage. A NOEL of 30 ppm (71 mg m⁻³) can be identified for systemic toxicity via inhalation exposure. Repeated oral administration caused reduced body weight gain and gastric irritation. No data are available on the toxicity of propylene oxide following repeated dermal exposure. The absence of significant toxic sequelae distant from the site of application following inhalation or oral administration suggests that concerns about target organ toxicity can be focused almost exclusively on tissues at the sites of initial contact.

Propylene oxide is clearly a direct-acting mutagen *in vitro* and animal data indicate that it can produce somatic cell mutation *in vivo*, particularly in the tissues at the site of contact. In relation to the potential of propylene oxide to cause germ cell mutation, negative results were obtained in dominant lethal studies by relevant routes of exposure. There are no other data relating to the ability of propylene oxide to cause heritable mutations in germ cells; toxicokinetic data indicate that propylene oxide can reach the testes following a physiological route of administration. Given that propylene oxide is a direct-acting mutagen then the possibility that it might express this activity within the germ cells cannot be discounted.

Propylene oxide is a respiratory tract carcinogen in animals and it is presumed that the mechanism of carcinogenesis involved is relevant to human health. It is possible that inflammation is a key influence in the production of cancer, and in this regard it is noteworthy that typical occupational exposures are an order of magnitude below the levels at which respiratory tract irritation is observed in rats. It is not known whether the carcinogenic mechanism can arise in the absence of chronic inflammation. It is not currently possible to determine a threshold for mutagenic events and so it is not possible to identify a threshold for carcinogenicity. Therefore, it is not possible to identify a safe level of exposure at which there would be no risk to human health.

There is no evidence for any adverse effect of propylene oxide on fertility or development.

4.1.3 Risk characterisation

Workers

It is not possible to identify a level of exposure at which there would be no cause for concern for human health for the endpoints of carcinogenicity and mutagenicity. Therefore, **conclusion (iia)** is reached for workers for these endpoints. This conclusion is dependent upon the industry continuing to implement new procedures to reduce exposure when possible.

Any indication that this is not occurring would prompt a review of the risk assessment and might result in a revision of the conclusion to allow for the development of a risk reduction strategy.

Conclusion (iia) Risks cannot be excluded for all other exposure scenarios, as the substance is identified as a non-threshold carcinogen. The adequacy of existing controls and the feasibility and practicability of further specific measures should be considered. However, the risk assessment indicates that risks are already low. This should be taken into account when considering the adequacy of existing controls and the feasibility and practicability of further specific risk reduction measures.

Consumers

Conclusion (iia) is reached because it is not currently possible to determine a threshold for mutagenic or carcinogenic events. Therefore, it is not possible to identify any level of exposure at which there would be no risk to human health. It is, however, noted that exposures are extremely low and therefore that the degree of risk is anticipated to be negligible.

Conclusion (iia) Risks cannot be excluded for all other exposure scenarios, as the substance is identified as a non-threshold carcinogen. The adequacy of existing controls and the feasibility and practicability of further specific measures should be considered. However, the risk assessment indicates that risks are already low. This should be taken into account when considering the adequacy of existing controls and the feasibility and practicability of further specific risk reduction measures.

Humans exposed via the environment

Conclusion (iia) is reached for mutagenicity and carcinogenicity because it is not currently possible to determine a threshold for these events. Therefore, it is not possible to identify any level of exposure at which there would be no risk to human health. Risk reduction measures which are already being applied should be taken into account. It is, however, noted that exposures in local and regional scenarios are extremely low and therefore that the degree of risk is anticipated to be very low.

Conclusion (iia) Risks cannot be excluded for all other exposure scenarios, as the substance is identified as a non-threshold carcinogen. The adequacy of existing controls and the feasibility and practicability of further specific measures should be considered. However, the risk assessment indicates that risks are already low. This should be taken into account when considering the adequacy of existing controls and the feasibility and practicability of further specific risk reduction measures.

Combined exposure

A worst-case combined exposure scenario is composed of exposure in the workplace and to the highest local environmental exposure levels. No quantitative estimate of total exposure from inhalation, dermal and oral routes, is possible. For the main endpoints of concern, mutagenicity and carcinogenicity, no threshold of exposure below which there would be no cause for concern to human health can be identified. However, exposure is very low. In both cases of worker and exposure via the environment **conclusion (iia)** is appropriate.

Conclusion (iia) Risks cannot be excluded for all other exposure scenarios, as the substance is identified as a non-threshold carcinogen. The adequacy of existing controls and the feasibility and practicability of further specific measures should be considered. However, the risk assessment indicates that risks are already low. This should be taken into account when considering the adequacy of existing controls and the feasibility and practicability of further specific risk reduction measures.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

Propylene oxide is a highly flammable gas that has a large vapour pressure at ordinary temperature. It is also explosive over a wide range of concentrations when mixed with air. Current controls are considered sufficient and therefore **conclusion (i)** is reached.

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

5 RESULTS

Production of propylene oxide in the EU is estimated to be 1,445,000 tonnes per year, with an extra 50,000 tonnes imported. It is largely used as a monomer in polymer production or as an intermediate in the synthesis of other substances. A small proportion is used directly as a stabiliser.

5.1 ENVIRONMENT

Local releases of propylene oxide to the environment may occur during production and use. These releases have been quantified in the assessment and used to calculate PECs for various environmental compartments.

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

This applies to the aquatic (surface water and sediment) and terrestrial compartments for both production and use. Although a PNEC could not be derived, no risks are expected for sewage treatment plant or the atmosphere. An assessment of secondary poisoning is unnecessary based on the properties of the substance.

5.2 HUMAN HEALTH

5.2.1 Human health (toxicity)

Workers

Exposure to propylene oxide by any route represents a cause for concern to human health and must be properly controlled. The available information on occupational exposure indicates that exposure to propylene oxide is stringently controlled, to the limits of technology that is currently available. As a substance for which no thresholds have been identified below which there would be no cause for concern for human health for the endpoints of carcinogenicity and mutagenicity, **conclusion (iiia)** is reached for workers for these endpoints. This conclusion is dependent upon the industry continuing to implement new procedures to reduce exposure when possible.

Any indication that this is not occurring would prompt a review of the risk assessment and might result in a revision of the conclusion to allow for the development of a risk reduction strategy.

Conclusion (iiia) Risks cannot be excluded for all other exposure scenarios, as the substance is identified as a non-threshold carcinogen. The adequacy of existing controls and the feasibility and practicability of further specific measures should be considered. However, the risk assessment indicates that risks are already low. This should be taken into account when considering the adequacy of existing controls and the feasibility and practicability of further specific risk reduction measures.

It is not possible to characterise the risk to workers for skin sensitisation therefore no formal conclusion has been reached.

Consumers

Conclusion (iia) is reached because it is not currently possible to determine a threshold for mutagenic events or, therefore, for carcinogenic events. Therefore, it is not possible to identify any level of exposure at which there would be no risk to human health. It is, however, noted that due to the half-life of 30-40 h and use in consumer products at very low concentrations, exposures to consumers are extremely low and therefore that the degree of risk is anticipated to be negligible.

Conclusion (iia) Risks cannot be excluded for all other exposure scenarios, as the substance is identified as a non-threshold carcinogen. The adequacy of existing controls and the feasibility and practicability of further specific measures should be considered. However, the risk assessment indicates that risks are already low. This should be taken into account when considering the adequacy of existing controls and the feasibility and practicability of further specific risk reduction measures.

Humans exposed via the environment

Humans are exposed indirectly via the environment via several sources, the principal source being drinking water. As it is not currently possible to determine a threshold for mutagenic or carcinogenic events, it is not possible to identify any level of exposure at which there would be no risk to human health. It is, however, noted that exposures in local and regional scenarios are extremely low and that the degree of risk is anticipated to be very low. Therefore, **conclusion (iia)** applies.

Conclusion (iia) Risks cannot be excluded for all other exposure scenarios, as the substance is identified as a non-threshold carcinogen. The adequacy of existing controls and the feasibility and practicability of further specific measures should be considered. However, the risk assessment indicates that risks are already low. This should be taken into account when considering the adequacy of existing controls and the feasibility and practicability of further specific risk reduction measures.

Combined exposure

A worst-case combined exposure scenario is composed of exposure in the workplace and to the highest local environmental exposure levels. No quantitative estimate of total exposure from inhalation, dermal and oral routes, is possible. For the main endpoints of concern, mutagenicity and carcinogenicity, no threshold of exposure below which there would be no cause for concern to human health can be identified. However, exposure is very low. In both cases of worker and exposure via the environment **conclusion (iia)** is appropriate.

Conclusion (iia) Risks cannot be excluded for all other exposure scenarios, as the substance is identified as a non-threshold carcinogen. The adequacy of existing controls and the feasibility and practicability of further specific measures should be considered. However, the risk assessment indicates that risks are already low. This should be taken into account when considering the adequacy of existing controls and the feasibility and practicability of further specific risk reduction measures.

5.2.2 Human health (risk from physico-chemical properties)

There are hazards associated with the extremely low flash point, high vapour pressure and flammability of this substance. However, during the manufacture, storage and use of this substance the stringent control measures used ensure that risks arising from the physicochemical properties are small.

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

