EUROPEAN COMMISSION

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n-PENTANE

CAS No: 109-66-0

EINECS No: 203-692-4

Summary Risk Assessment Report

2003 **Special Publication I.03.152**

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SUMMARY RISK ASSESSMENT REPORT

Final report, 2003

Norway

This document has been prepared by the Norwegian Pollution Control Authority in consultation with the Directorate of Labour Inspection, on behalf of the European Union. The scientific work has been prepared by the National Institute of Public Health, the Norwegian Institute for Water Research (NIVA) and the National Institute of Occupational Health.

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Date of Last Literature Search:	**1996**
Review of report by MS Technical Experts finalised:	**2002**
Final report:	**2003**

(The last full literature survey was carried out in 1996, targeted searches have been carried out subsequently for example on trophospheric ozone formation. Toxicity data have been added up until 2001).

PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance n-pentane that has been prepared by Norway 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 comprehensive Final Risk Assessment Report (Final RAR) that can be obtained from the European Chemicals Bureau[1]. The Final RAR should be used for citation purposes rather than this present Summary Report.

[1] European Chemicals Bureau – Existing Chemicals – http://ecb.jrc.it

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1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS No:	109-66-0
EINECS No:	203-692-4
IUPAC name:	n-pentane
Synonyms:	pentane, normal pentane
Molecular weight:	72.15 g/mole
Molecular formula:	C_5H_{12}
Structural formula:	CH_3-CH_2-CH_2-CH_2-CH_3

1.2 PURITY/IMPURITIES, ADDITIVES

Purity: > 95%

Impurities: Butane, isopentane and cyclopentane, that are present at concentrations in the range from a few ppm up to a few percent.

Additives: No additives declared in IUCLID.

1.3 PHYSICO-CHEMICAL PROPERTIES

The physico-chemical properties of n-pentane are summarised in **Table 1.1**. All further calculations will be performed using these values.

Table 1.1 Physico-chemical properties

Property	Value	Method / reference
Physical state	liquid	-
Boiling point	36°C	D1078 ASTM
Melting point	-130°C	D2386 ASTM
Vapour pressure	56,580 Pa at 20°C	Solvent Guide (C. Marsden, 2nd edition)
Water solubility	38.5 mg/l at 20C	The Merck Index (The Merck Index of Chemicals and Drugs 6th edition)
Partition coeff	3.45 log Kow	Several methods
Density	626 kg/m^3 at 20°C	The Merck Index (The Merck Index of Chemicals and Drugs 6th edition)
Surface tension	16.05 mN/m at 20°C	Jasper (1972)
Flash point	-46°C	Solvent Guide (C. Marsden, 2nd edition)
Autoignition	285°C	E659 ASTM
Vapour density/air	2.49	Exxon Chemical
Henry's Constant	106,030	Calculated

For full references, see comprehensive risk assessment report (http://ecb.jrc.it)

1.4 CLASSIFICATION

The classification/labelling in Annex I is (according to 25th ATP):

Classification	F+; R12 * Xn; R65-R66-R67 N; R51/53
Labelling	F+; Xn; N R: 12-65-66-67-51/53 S: (2-)9-16-29-33-61-62

F+ indicates:	Extremely flammable.
Xn indicates:	Harmful.
N indicates:	Dangerous for the environment
R12 states:	Extremely flammable.
R65 states:	Harmful: may cause lung damage if swallowed.
R66 states:	Repeated exposure may cause skin dryness or cracking.
R67 states:	Vapours may cause drowsiness and dizziness.
R51/53 states:	Toxic to aquatic organisms; May cause long-term adverse effects in the aquatic environment.
S2 states:	Keep out of the reach of children.
S9 states:	Keep container in a well-ventilated place.
S16 states:	Keep away from sources of ignition – No smoking.
S29 states:	Do not empty into drains.
S33 states:	Take precautionary measures against static discharges.
S61 states:	Avoid release to the environment. Refer to special instructions/safety data sheets.
S62 states:	If swallowed do not induce vomiting: seek medical advice imeediately and show the container or label.

Nota C.

(* The EU Classification and Labelling group has decided that iso-pentane and pentane (n-pentane) should be kept as one entry, this had the consequence that the change that was agreed in the classification for iso-pentane to "Extremely flammable" (R12) also became valid for n-pentane.)

2 GENERAL INFORMATION ON EXPOSURE

Normal pentane is a constituent of crude oil and a component of the condensate from natural gas production. Normal pentane is primarily obtained by fractional distillation of a petroleum stream (generally light virgin naphtha) obtained from processing of crude oil. It is produced through a closed batch process in petroleum refineries or petrochemical plants. The use of highly efficient distillation equipment allows isolation of n-pentane of qualities of purity between 80% and up to 99% by weight.

There are 6 companies producing n-pentane in the European Union. The total production is 55 ktonnes for the year 1994. Export of n-pentane is roughly equal to imports. It was assumed that 50 ktonnes were used within EU.

Normal pentane is used mainly (approximately 70%) as a foaming agent in the expansion of polystyrene and polyurethane. It is also used as a solvent in aerosols (about 14%) and a solvent in polymerisation process (about 16%). In all of these uses n-pentane is unreacted and therefore susceptible to release to the environment. Some of these use categories include containment or incineration of spent n-pentane. However the risk assessment report estimates that about 80% of used n-pentane is released into the air compartment. There are a few minor uses, these include use as a laboratory chemical, solvent in adhesives and “other uses”.

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

It should be noted that this risk assessment only covers the n-pentane emissions from sources related to the life cycle of commercially produced n-pentane (isolated n-pentane). Normal pentane is also a constituent of crude oil and petroleum products like gasoline. These sources are not covered in this risk assessment, however a rough estimate is made with respect to the release and contribution from gasoline to environmental concentrations.

3.1.1 Environmental fate

Due to the physical-chemical properties n-pentane released into the environment mainly ends up in the atmospheric compartment according to the Mackay level 1 model. In the aquatic environment n-pentane is expected to be stable to hydrolysis and photodegradation. Normal pentane is readily biodegradable, meeting the 10-day window criterion. In air n-pentane is exposed to indirect photolysis by photochemical oxidative degeneration with an estimated half-life of approximately 4 days.

Normal pentane has a moderate adsorption capacity with an estimated Koc of 784 l/kg. Normal pentane has a log Kow of 3.45 and a calculated BCF of 171 l/kg, indicating a potential for bioaccumulation. Due to rapid degradation and elimination bioconcentration of n-pentane in the food chain is not expected.

3.1.2 Environmental concentrations

Most of the identified releases are to air. EUSES has been used to calculate local, regional and continental PECs for all life cycle steps. Where site-specific release data are available local PECs have been calculated manually.

With respect to production sites no emission to water is expected, the highest estimated local PEC_{air} is 140 µg/m^3. Similarly, for processing, for use as a foaming agent, no direct emission to water takes place and the highest estimated local PEC_{air} is 259 µg/m^3. The highest estimated local PEC_{air} is 610 µg/m^3 for formulation of polymer diluent. With respect to the water compartment the use of n-pentane as a laboratory chemical gave the highest calculated PEC in water equal to 1.4 µg/l. No known direct emissions to soil were identified, soil mainly being contaminated via depositions and sludge application.

The estimated regional PEC_{air} is 0.32 µg/m^3. This value is based on the releases from isolated n-pentane only. The release of n-pentane from car fuel in the EU was roughly estimated to be 224 tonnes/day, and adding 1/10 of this volume to the regional emissions of n-pentane would give a $PECregional_{air}$ of 0.84 µg/m^3.

The major source of n-pentane air concentrations in the cities can be assumed to be car fuel. Recent data from the UK indicate air concentrations in cities in the range 1 - 14 µg/m^3. In a monitoring study close to a city road side (Copenhagen) n-pentane was found in the range 1.2 - 17.1 µg/m^3.

<u>Potential creation of ozone due to n-pentane</u>

Normal pentane contributes to VOC and to the formation of tropospheric ozone. The creation of trophospheric ozone is dependent on a number of factors like the VOC speciation and concentrations, VOC/NOx ratio, solar radiation and meteorological conditions. The environmental conditions differ considerably within Europe and a certain concentration of VOC may lead to very different ozone concentrations. Furthermore the VOC composition will be highly variable and depend on the industrial sources, traffic emissions and natural sources. The contribution from isolated n-pentane will therefore depend on the composition of local and regional industry. It was estimated that the emission of n-pentane from the use and production of isolated n-pentane may be in the order of 0.16 – 0.4% of the total NMVOC emissions.

3.2 EFFECTS ASSESSMENT

3.2.1 Aquatic compartment (incl. sediment)

Relatively few acute studies of acceptable quality were available and there were no long-term studies. Because of rapid degradation and evaporation several tests were considered to be invalid due to uncertainties with respect to the exposure concentrations. Toxicity studies are available for all trophic levels of aquatic species. The acute toxicity to fish *Oncorhynchus mykiss* was LC50 4.26 mg/l. The lowest valid acute toxicity for invertebrates *Daphnia magna* was 2.7 mg/l. The EC50 for growth inhibition for the algae *Selenastrum capricornutum* based on growth rate was 10.7 mg/l. The range of acute effects was supported by QSAR estimated values for fish, crustacean and algae. Based on the chemical structure of n-pentane and since QSAR data are in agreement with the short-term toxicity data, it is considered that the toxic mode of action is by non-polar narcosis. An assessment factor of 100 was used to calculate the predicted no effect concentration (PNEC) for n-pentane in the aquatic environment, which gives a $PNEC_{aquatic}$ = 27 µg/l.

No information is available for the toxicity to microorganisms or terrestrial organisms. PNECs for the sediment and terrestrial compartments were derived by the equilibrium partitioning method.

3.2.2 Atmosphere

Normal pentane is rapidly removed from the air compartment through photodegradation and reaction with OH-radicals, a half-life in air of approximately 4 days was estimated. The compound is therefore not expected to contribute significantly to global warming.

No direct toxicity data on plants are available.

Normal pentane contributes to VOC and to the formation of tropospheric ozone, which is toxic to green plants, animals and humans. The vegetation and wildlife may be severely affected by ozone incidences. The relation between ozone precursors in terms of VOCs and ozone formation is complicated and depends on the speciation and concentrations of VOC, NO_x, solar radiation and OH-radicals. It is estimated that n-pentane has a POCP (Photochemical Ozone Creation Potential) of 30 - 40 relative to ethylene which has a POCP of 100.

3.2.3 Secondary poisoning

With a log Kow of 3.4 n-pentane has a potential for bioconcentration. However, n-pentane is rapidly degraded and eliminated (see health section) and bioconcentration in the food chain is therefore not expected. The major route of exposure of organisms higher up in the food chain is likely to be directly through air.

3.3 RISK CHARACTERISATION

It should be noted that this risk assessment covers the risks associated with the life cycle of n-pentane. The risks connected to the presence of n-pentane in other EINECS substances, particularly petroleum products (non-isolated n-pentane) have not been assessed.

3.3.1 Aquatic compartment (incl. sediment)

There is no direct release to water of n-pentane during production or use except for a few minor uses. Most of the exposure of surface water is indirectly through deposition as calculated by EUSES for the regional $PEC_{aquatic}$. The risk assessment for the aquatic compartment also applies for sediment as both PEC and PNEC for sediment are estimated using the equilibrium partitioning method. The regional PEC/PNEC is $1.37 \cdot 10^{-4}$. Highest estimated PEC/PNEC is 0.051 with respect to use of n-pentane as a laboratory chemical. **Conclusion (ii).**

3.3.2 Atmosphere

A PNEC has not been calculated for the atmosphere, as no direct toxicity data for pentane on terrestrial plants are available. Plant toxicity data from n-hexane and cyclohexane and the molecular structure of n-pentane do not indicate that toxicity on terrestrial plants is of concern. More information and further assessment in this respect is therefore not considered necessary: **conclusion (ii)**.

This conclusion applies to plants exposed via air.

In order to evaluate n-pentane contribution to VOC and the formation of tropospheric ozone it has been estimated that the emission of n-pentane from the use and production of isolated n-pentane may be in the order of 0.16 – 0.4% of the total NMVOC emissions. In general isolated n-pentane only contributes to a small extent. However, this is one substance among hundred of different VOCs and the contribution of 0.16 - 0.4% from a single substance may therefore not be negligible. Moreover it has to be emphasised that the local and regional NMVOC composition may have a higher contribution from isolated n-pentane than indicated by the average calculations due to differences in local NMVOC sources: **conclusion (iii)**.

This conclusion applies in the context of the Council Regulation (EEC) 793/93 of Existing Substances to the contribution of isolated n-pentane to the formation of ozone and other harmful substances i.e. smog formation. Therefore, in the context of the consideration of which risk reduction measures that would be the most appropriate, it is recommended that under the relevant air quality Directives a specific in-depth evaluation be performed. Such an evaluation should focus on the contribution of isolated as well as non-isolated n-pentane to the complex issue of ozone and smog formation and the resulting impact on air quality.

3.3.3 Terrestrial compartment

All PEC/PNEC values for soil are well below 1: **conclusion (ii)**.

3.3.4 Secondary poisoning

Normal pentane has a log Kow of 3.45 and calculation according to the TGD gives a BCF of 171 l/kg. Normal pentane therefore shows a potential for biomagnification through the food chain. However, n-pentane is neither classified as toxic or very toxic, nor with any of the risk phrases R 40, 45, 46, 48, 60 -63. Furthermore studies with mammels indicate that n-pentane is rapidly degraded and eliminated. Therefore it is not considered necessary to carry out a risk characterisation for secondary poisoning: **conclusion (ii)**.

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

4.1.1.1 Occupational exposure

Occupational exposure may occur during the production of n-pentane and in downstream uses of the substance. The main applications are as a foaming agent, as a constituent in aerosols and as an organic solvent for miscellaneous purposes. Exposure to n-pentane from gasoline production/handling or filling is not part of this risk assessment.

For occupational exposure, inhalation is the predominant route of exposure, while oral contact is considered negligible. The dermal exposure time is usually short because of n-pentane high volatility (boiling point 36°C). However, if e.g. hands are covered with liquid n-pentane, then dermal absorption occurs. Because no measured data are available on dermal exposure, exposure to n-pentane is estimated with the dermal model of EASE.

The scenarios considered for occupational exposures to n-pentane are presented below, and are selected on the basis of the information given by the industry.

Scenario 1 Production of n-pentane
Scenario 2 Industrial use of products containing n-pentane
- Scenario 2A: Production of polystyrene granulates (formulation)
- Scenario 2B: EPS (expanded polystyrene) manufacturing (processing)
- Scenario 2C: Production of rigid polyurethane foam
- Scenario 2D: Manufacturing of aerosol-containers

Scenario 3 Professional end use of products containing n-pentane
- Scenario 3A: Hair salons
- Scenario 3B: Professional use of car-care products
- Scenario 3C: Miscellaneous applications

The term "exposure data" is used for both personal sampling and stationary sampling data. Air concentration data are given in mg/m^3.

Table 4.1 OEL values or administrative norms for n-pentane in some countries

Country	Year	OEL values or adm.norms (short-time value)	
		mg/m^3	ppm
Norway (adm. norm)	2000	750	250
Sweden	2000	1,800 (2,000)	600 (750)
Denmark (all isomers)	2000	1,500	500
Finland	2000	1,500 (1,900)	500 (630)
The Netherlands	1997-1998	1,800	600
Germany MAK (all isomers)	1999	2,950	1,000
United Kingdom	EH40/2000	—	—
ACGIH	1999	1,770	600
Japan	1998-1999	880	300

Table 4.2 Summary of exposure levels for occupational exposure of n-pentane taken forward to the risk characterisation

Workplace operation	Inhalation (mg/m³)	Short time value (mg/m³)	Dermal (mg/person/day)
Scenario 1: Production of n-pentane	typical value: 66.5 reasonable worst-case: 180	599	420 (E)
Scenario 2: Industrial use of products containing n-pentane	typical value: 269 reasonable worst case: 338	643	84 (E)
Scenario 3: Professional end-use of products containing n-pentane	typical value: 35 reasonable worst case: ~198	not relevant	negligible because of the low boiling point

Abbreviations: E = EASE

4.1.1.2 Consumer exposure

It is assumed that the main exposure in the EU to n-pentane is from the use of aerosol products. This exposure covers a range of products, however, the most important consumer exposure is connected with the use of hairsprays, antiperspirants, paints, and car care products (European Aerosol Federation, 1996). The major exposure determinants are the "spray time" and the dynamics of the environment in which the product is used.

Hairspray count for 50% of total consumer use of aerosols, where the weight fraction of n-pentane is 40%. The highest exposure to n-pentane is therefore assumed to result from the normal use of hairspray in a confined space, e.g. poorly ventilated bathroom. A consumer exposure estimate for n-pentane in aerosols in hairsprays has been made according to the TGD, and the inhaled dose was calculated to be 7.8 mg/kg/day. Furthermore, an empirical estimate and a worst-case exposure scenario have been performed, and the inhaled doses were calculated to be 2.75 mg/kg/day and 10.3 mg/kg/day, respectively. These values are used in the risk characterisation.

4.1.1.3 Humans exposed via the environment

Due to the physico-chemical properties of n-pentane, the only important exposure of the general population to n-pentane via the environment is in air. The local predicted environmental concentrations (PEClocal) in air at production sites 100 m from sources, are estimated to range from 0.0048 to 0.140 mg/m^3. This corresponds to an inhalation dose in humans from 1.37 to 40.0 µg/kg/day [when it is estimated that the volume air inhaled in humans is 20 m^3/day (TGD value), the human body weight is 70 kg (TGD value), and the exposure time is 24 hours]. The indirect exposure via environmental pathways given in µg/m^3 was calculated with the EUSES programme for different use patterns and life cycle stages. Based on these values the estimated exposure ranged from 0.174 to $9.1 \cdot 10^{-5}$ mg/kg/day**.**

4.1.2 Effects assessment

The toxicokinetics of n-pentane has been studied in *in vitro* and *in vivo* animal studies, and in human tissues. Oxidation *in vitro* of n-pentane to the alcohols 2-pentanol (83-89%) and 3-pentanol (11-16%) in the rat was observed to be the major pathway of n-pentane metabolism, and it was suggested that n-pentane was chiefly metabolised by microsomes. The skin penetration rate of n-pentane *in vitro* through excised abdominal full-thickness rat skin was shown to be 31.14 nmol/hour/cm^2. Compared to other aliphatic hydrocarbons (n-hexane, n-heptane, and n-octane) the skin penetration of n-pentane was considerably higher. A gas uptake study in rats indicated “a first order” of metabolic elimination below 100 ppm in the atmosphere. Concentrations higher than 100 ppm displayed saturation kinetics. An *in vivo* metabolism study in rats, where n-pentane was injected into a closed chamber system, showed that the major products of n-pentane metabolism appears to be CO_2, which indicates that n-pentane is metabolised *in vivo*. In humans, the tissue/air and blood/air partition coefficients were determined for several tissues. The highest tissue/air coefficient was measured in fat (39.6) and the lowest in heart (0.2). This is in accordance with n-pentane log $P_{ow} > 3$. Considering the rapid metabolism and excretion of n-pentane, tissue accumulation is considered to be low. In the risk characterisation 100% absorption is used for inhalation and dermal exposure to n-pentane.

n-Pentane is of low acute toxicity by inhalation, oral administration and i.v. application. In experimental animal studies neurobehavioral and neurotoxic effects are the major toxic endpoints reported. A recent acute toxicity study by oral intubation of n-pentane in rats revealed a LD50 > 2,000 mg/kg (limit test). At this dose level no treatment-related death or consistent signs of systemic toxicity were observed. The LC50 value of n-pentane after 2 hours exposure was reported to be approximately 295,000 mg/m^3 (98,662 ppm) in mice. The time taken to produce “light anaesthesia” was also investigated in this study, and anaesthetic effects were observed in mice after 1.3 minutes when exposed to 303,030 mg/m^3 (101,348 ppm) air concentrations of n-pentane. In another study light anaesthesia occurred from 96,000 mg/m^3, 5 min exposure in Swiss mice. In a recent study performed in accordance with GLP the behavioural effect of n-pentane was studied in rats after short-time inhalation exposure by using a standardised functional observational battery (FOB). In this study no effect of n-pentane on motor activity was reported after exposure up to 20,000 mg n-pentane/m^3 (6,800 ppm) for 8 hours per day for 3 days. On cognitive behaviour a mild and reversible effect of n-pentane was reported after exposure to 2,000 mg n-pentane/m^3 (675 ppm) and 6,500 mg n-pentane/m^3 (2,200 ppm) 8 hours per day 3 days, however, no effect was reported at 20,000 mg n-pentane/m^3. Neurotropic effects of n-pentane were observed in rats and mice exposed whole body to 62,790 and 70,265 mg/m^3 (21,000 ppm and 23,500 ppm) n-pentane, respectively.

Based on the values of the kinematic viscosity for n-pentane ($3.58 \cdot 10^{-7}$ m^2/s), n-pentane has the potential to cause chemical pneumonia and should be classified with R65.

The saturated vapour concentration of n-pentane is 1,585 mg/l. Pentane has caused narcotic effects in mice at a concentration of 96 mg/l and after 5 min exposure. Thus, the ratio of narcotic effect concentration to the saturated vapour concentration is 0.06 (i.e. less than 0.1 required for classification with R67). Based on this data n-pentane should be classified with R67.

n-Pentane was reported to be a mild skin irritant according to the Draize Method of scoring in White rabbits exposed dermally to 0.5 ml n-pentane. Transient injury to the conjunctiva was observed after ocular exposure to a single installation of 0.1 ml n-pentane, whereas no corneal or iridal responses were observed. There is suggestive evidence that n-pentane is a slight respiratory irritant in mice. In a Guinea Pig Maximisation test n-pentane did not show any sensitisation potential. From clinical experience in humans it is well known that solvents in general have a defatting action on the skin, which after repeated exposure may cause skin dryness and flaking. This may cause local skin reactions and enhancement in the penetration and uptake of toxic substances.

In a recent 13 week sub-chronic inhalation toxicity study in rats no systemic toxicity was observed following n-pentane exposure up to 20,000 mg/m^3 (6,660 ppm), and a NOAEL from this study was set at ≥ 20,000 mg/m^3 (6,660 ppm). This study was performed according to EC Guidelines and GLP conditions. In a 4-week oral nephrotoxicity screening study no histopathologic changes were noted in the kidneys of exposed rats up to 2,000 mg/kg bw. However, mortality was reported at 500 mg/kg bw/day (2/10) and at 2,000 mg/kg bw/day (4/10), and some animals were lethargic. Furthermore, stomach lesions were reported in some animals at 2,000 mg/kg bw/day. In a 16- and 30-week neurotoxicity study no neurotoxic effects were observed in rats after exposure to 8,970 mg/m^3 (3,000 ppm) n-pentane. In the risk characterisation a NOAEL of 20,000 mg/m^3 (6,660 ppm) is used.

n-Pentane is not considered to be mutagenic.

As regard carcinogenicity, no data were available.

No one- or two-generation study with n-pentane is available, however, in a 13-week subchronic inhalation toxicity study in male and female rats no signs of toxicity were observed on the reproductive system by macroscopic or microscopic evaluation after exposure to n-pentane up to 20,000 mg/m^3 (6,660 ppm). Therefore, no study investigating effects on fertility and/or the reproductive organs after exposure to n-pentane was recommended. In a developmental toxicity study in female rats the NOAEL was ≥ 1,000 mg/kg bw both for the dams and the offspring. No information on the potential of n-pentane to cause developmental toxicity in humans is available.

4.1.3 Risk characterisation

It should be noted that this risk assessment only covers the risks associated with the life cycle of n-pentane, with the EINECS No 203-692-4. Any risks connected to the presence of n-pentane in other EINECS substances, particularly petroleum products (non-isolated n-pentane), have not been assessed.

4.1.3.1 Workers

It is assumed that oral exposure is prevented by personal hygienic measures and the risk characterisation for workers is limited to the dermal and respiratory routes of exposure.

The quoted exposure data show low values compared to reported harmful concentrations of n-pentane, and the data represent normal work situations. It is likely to presume that some maintenance tasks, for example the maintenance of the processing equipment, can cause much higher exposure to workers. It is anticipated that personal protective equipment (PPE) is worn when performing maintenance of long duration. As a consequence of n-pentane highly flammable property, high concentrations are mostly avoided in the workplace.

Data on absorption in the lungs after inhalation is lacking. Therefore, 100% respiratory absorption is used as a default value.

Since there is no adequate knowledge about the absorption after dermal exposure of n-pentane, 100% absorption is used as a default value.

Acute toxicity

Inhalation

Given the low toxicity observed in the acute inhalation studies and the anticipated occupational exposure levels it is concluded that n-pentane is of no concern for workers with regard to acute effects: **conclusion (ii)**.

Irritation

Skin

The study results indicate that n-pentane should not be classified as a skin irritant. However, for solvents in general, it is well known from clinical experience in humans that they have a defatting action on the skin, and that continued exposure may lead to development of irritant contact dermatitis.

Dermal exposure is reduced due to the fast evaporation of n-pentane from the skin.

It is concluded that n-pentane is of no concern with respect to skin irritation: **conclusion (ii)**.

Eyes

Despite the mild irritation effects observed in the acute eye irritation study in rabbits, there is no evidence that n-pentane cause eye irritation in humans. Exposure to eyes in the workplace is possible via vapours or accidentally by splashing, but goggles are usually worn when the pure substance is handled and thus exposure to eyes is unlikely to occur: **conclusion (ii)**.

Inhalation

In an inhalation study in mice, concentrations up to 16,000 ppm (47,840 mg/m^3) produced no irritation or anaesthesia, and it is concluded that n-pentane is of no concern for workers with regard to respiratory irritation: **conclusion (ii)**.

Corrosivity

Given the results from the skin and eye irritation studies it is concluded that n-pentane is of no concern for workers with regard to corrosivity: **conclusion (ii)**.

Sensitisation

Skin

Given the results from the dermal sensitisation study with guinea pigs it is concluded that n-pentane is of no concern for workers with regard to skin sensitisation: **conclusion (ii)**.

Inhalation

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

Repeated-dose toxicity

The overall NOAEL of ≥ 20,000 mg/m^3 n-pentane from a 90-day repeated dose inhalation toxicity study is used in the risk characterisation, and the NOAEL for inhaled dose of n-pentane is calculated to 1,766 mg/kg/day based on the exposure conditions in the rat study.

Inhalation

The highest measured level of n-pentane was found at the storage site for EPS blocks and hence this is the worst-case scenario.

Table 4.3 Inhalation MOSs calculated for repeated dose toxicity as a critical effect for each scenario (Exxon Biomedical Sciences, 1997)

Occupational scenario	**Air concentration (mg/m³)**			**MOS (NOAEL/measured value)**		
	Typical Value	**RWC**	**Short-term value**	**Typical value**	**RWC**	**Short-term value**
Scenario 1: Production of n-pentane	66.5	180	599	≥ 300	≥ 111	>33
Scenario 2: Industrial use of products containing n-pentane (EPS production)	269	338	643	≥ 74	≥ 59	> 31
Scenario 3: Professional end-use of products containing n-pentane (Hair salons)	35	~ 198	Not relevant	≥ 571	≥ 101	Not relevant

NOAEL is ≥ 20,000 mg/m³
RWC = reasonable worst-case value

Skin

Table 4.4 MOS calculated for dermal exposure with the repeated dose toxicity as a critical effect

Exposure scenario	**Dermal (mg/kg/day)**	**NOAEL (calculated internal dose) (mg/kg/day)**	**MOS**
Scenario 1: Production of n-pentane	6	1,766	≥ 294
Scenario 2: Industrial use of products containing n-pentane	1.2	1,766	1,472
Scenario 3: Professional end-use of products containing n-pentane	Negligible	1,766	High

Combined route

Table 4.5 Combined MOS calculated for repeated dose toxicity as a critical effect for the scenarios (reasonable worst case)

Exposure scenario	Inhalation 1)		Dermal (mg/kg/day)	Combined route mg/kg/day)	MOS
	External (mg/m^3)	Internal (mg/kg/day)			
Scenario 1: Production of n-pentane	180	25.7	6	31.7	≥ 56
Scenario 2: Industrial use of products containing n-pentane	338	48.3	1.2	49.5	> 36
Scenario 3: Professional end-use of products containing n-pentane (Hair salons)	~ 198	28.3	Negligible	28.3	> 101

The NOAEL for inhaled dose of n-pentane is calculated to 1,766 mg/kg/day
1) Reasonable worst-case value

The real margin of safety is likely to be substantially higher taking into consideration that the NOAEL of 20,000 mg/m^3 probably is too low and the uptake of n-pentane in the lungs is less than 100% and the duration of the exposure will likely be << 8 hours a day. Also, because of the high volatility of n-pentane the dermal uptake is expected to be low. Taking this into consideration, together with the lowest MOS-values (reasonable worst case) of ≥ 59 for the inhalation exposure and ≥ 36 for the combined route based on internal dose, **conclusion (ii)** for the worst-case scenario (scenario 2) is chosen.

Mutagenicity

n-Pentane was not positive in any of the studies reported on mutagenicity, and it is concluded that n-pentane is of no concern in regard to mutagenicity: **conclusion (ii)**.

Carcinogenicity

There are no data available on carcinogenicity of n-pentane. Given that the substance is not genotoxic and that there are no case reports on carcinogenic effects suspecting n-pentane to be the cause, it is considered that n-pentane is of no concern in regard to carcinogenicity: **conclusion (ii)**.

Toxicity for reproduction

No sign of toxicity was observed on the reproductive system after exposure to n-pentane up to 20,000 mg/m^3 in a 13-week sub-chronic inhalation study. In a developmental toxicity study in female rats exposed to n-pentane by oral gavage from gestation day 6-15, the NOAEL was ≥1,000 mg/kg/day for dams and offspring. It is concluded that n-pentane is of no concern: **conclusion (ii)**.

4.1.3.2 Consumers

Consumers may be exposed by inhalation to n-pentane mainly by the use of hairspray, antiperspirants, paints and car care products. Since the major exposure to n-pentane is related to the use of hairspray, the inhalation dose was only calculated for this exposure scenario.

The inhalation dose from a TGD estimate is calculated to be 7.8 mg/kg/day, from an empirical estimate 2.75 mg/kg/day, and from a worst-case exposure estimate 10.3 mg/kg/day. The overall NOAEL to be used is ≥ 20,000 mg/m^3 n-pentane from a 90-day repeated dose inhalation toxicity study corresponding to an internal dose at 1,766 mg/kg/day (rat) when it is estimated that the volume inhaled in rat is 4.4 L/hour, inhalation time is 6 hours (see study description), and the rat body weight is 0.3 kg. This gives a MOS value greater than 226 for the TGD estimate, a MOS greater than 642 for the empirical estimate, and a MOS for the worst-case estimate greater than 171. These MOS values are only estimates, and the most reliable MOS value is greater than 642 (empirical estimate), since in the TGD estimate it is assumed that the exposure time is 6 min, which is a really long hairspray time.

No concern for consumers is expected: **conclusion (ii).**

4.1.3.3 Humans exposed via the environment

The only important exposure of the general population to n-pentane via the environment is from air. The local predicted environmental concentrations (PEClocal) in air are estimated to range from 0.0048 to 0.140 mg/m^3. These levels correspond to an inhalation dose in humans from 1.37 to 40.0 µg/kg/day. The indirect exposure via environmental pathways given in µg/m^3 was calculated with the EUSES programme for different use patterns and life cycle stages. Based on these values the estimated exposure ranged from 0.174 to $9.1 \cdot 10^{-5}$ mg/kg/day**.** Using a NOAEL at ≥ 20,000 mg/m^3 n-pentane from a 90-day repeated dose inhalation toxicity study, corresponding to an internal dose at 1,766 mg/kg/day (rat), the MOS values calculated from PEClocal ranged from $4.4 \cdot 10^4$ to $1.3 \cdot 10^6$. The MOS values based on EUSES estimations ranged from $1.0 \cdot 10^4$ to $1.9 \cdot 10^7$. Accordingly, the MOS values calculated from PEClocal and indirect exposure based on EUSES calculations are considered sufficient.

The substance is of no concern in relation to indirect exposure via the environment: **conclusion (ii).**

It is known that n-pentane contributes to tropospheric volatile organic compounds (VOC) and contributes to the tropospheric formation of ozone. The photochemically formation of ozone and other compounds depends on emission of all VOCs and other compounds in a complex interaction with other factors. The industrial use of the commercial product n-pentane contributes significantly to the overall emission of n-pentane, however, emission of n-pentane from car fuels and exhaust gases seem to be the largest single source. This risk assessment does not cover non-isolated n-pentane. It has been estimated that the emission of n-pentane from the use and production of isolated n-pentane may be in the order of 0.16 – 0.4% of the total non-methane (NM) VOC emissions.

Ozone exposure has been documented to give rise to severe effects in humans. The EU populations have experienced exceedance of the current EU threshold for health protection (110 µg/m^3, 8 hours average, directive 92/72/EEC), and the severity of exceedance of the EU threshold for health protection has been estimated by WHO (1999). When the WHO estimates are used to estimate the impact of emissions from the production and use of isolated n-pentane through formation of ozone, then this emission may very roughly have caused around 3-15 deaths in the summer of 1995, if a linear relationship exists between the emission of n-pentane, the emission of NMVOCs and the creation of ozone. However, no simple relationship has been established between the proportion of n-pentane to total NMVOC emitted - and thus also between emissions arising from the use of the commercial product n-pentane - and the creation of tropospheric ozone. One should also keep in mind that it is the combination of NOx and VOC and other factors that causes tropospheric ozone formation, and that cars are the main source of NMVOC compounds in cities.

However, based on this risk reduction measures seem necessary to consider a **conclusion (iii)**. This conclusion applies in the context of the Regulation of Existing Substances to the contribution of the commercial product (isolated) n-pentane to the formation of ozone. Considering the most appropriate risk reduction measures, it is recommended that under the relevant air quality Directives a specific in-depth evaluation be performed. Such an evaluation should focus on the contribution of isolated as well as non-isolated n-pentane to the complex issue of ozone and smog formation and the resulting impact on air quality.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

4.2.1 Exposure assessment

n.a.

4.2.2 Effects assessment

Based on the structure of the molecule n-pentane is not expected to have explosive properties as such. However, n-pentane is a volatile liquid and a mixture of air and n-pentane may burn explosively. Its explosive limits in air range from 1.4% (Lower Explosive Limit) to 8% (Upper Explosive Limit) by volume.

Normal pentane can accumulate static charges which can cause an incendiary electrical discharge (ignition source).

According to Annex I to Directive 67/548/EEC n-pentane is classified as Extremely flammable, F+; R12. No oxidizing properties are expected based on the structural formula.

4.2.3 Risk characterisation

Regarding physico-chemical properties flammability is of concern for n-pentane since it is a volatile liquid which is highly flammable and can form explosive mixtures with air.

In production and occupational use the flammability risk is not of concern provided that adequate measures are taken. According to the EU classification, packaging and labelling directives information about the flammability hazard must be provided on the label and in the safety data sheets.

Concerning use by consumers, information about the flammability hazard and precautionary measures must be given by a label on the product. In the EU, symbol, risk phrases and safety phrases are used for labelling of extremely flammable substances and preparations.

Furthermore the electrostatic accumulation hazard is of concern for n-pentane. Facilities must be designed to avoid possible ignition by static discharge, for example by earthing of equipment. According to the EU classification, packaging and labelling directives, particularly the provisions concerning safety data sheets, information about the risks and about precautionary measures during storage and handling must be given in the safety data sheet. Provided that the information is given and adequate measures are taken the risk of static charges and electric discharges (ignition source) is not of concern: **conclusion (ii)**.

5 RESULTS

5.1 ENVIRONMENT

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

This conclusion is reached for the atmosphere because of the contribution of isolated n-pentane to the formation of ozone and other harmful substances i.e. smog formation.

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 conclusion applies to the aquatic environment and the terrestrial compartment. All PEC/PNEC values for the aquatic environment and the terrestrial compartment are below 1, indicating no cause for concern.

5.2 HUMAN HEALTH

5.2.1 Human health (toxicity)

Workers

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.

Consumers

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.

Humans exposed via the environment

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

This conclusion is reached because of the contribution of isolated n-pentane to the formation of ozone and other harmful substances i.e. smog formation.

5.2.2 Human health (risks from physico-chemical properties)

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.