Institute for Health and Consumer Protection
Toxicology and Chemical Substances (TCS)
European Chemicals Bureau
I-21027 Ispra (VA) Italy

2-NITROTOLUENE

CAS No: 88-72-2

EINECS No: 201-853-3

Summary Risk Assessment Report

2008 **EUR 23517 EN/2**

The mission of the IHCP is to provide scientific support to the development and implementation of EU polices related to health and consumer protection. The IHCP carries out research to improve the understanding of potential health risks posed by chemical, physical and biological agents from various sources to which consumers are exposed.

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European Commission
Directorate-General Joint Research Centre
Institute of Health and Consumer Protection (IHCP)
European Chemicals Bureau (ECB)

Contact information:

Institute of Health and Consumer Protection (IHCP)
Address: Via E. Fermi 2749 – 21027 Ispra (Varese) – Italy
E-mail: ihcp-contact@jrc.it
Tel.: +39 0332 785959
Fax: +39 0332 785730
http://ihcp.jrc.cec.eu.int/

European Chemicals Bureau (ECB)
E-mail:esr.tm@jrc.it
http://ecb.jrc.ec.europa.eu/

Directorate-General Joint Research Centre
http://ec.europa.eu/dgs/jrc/

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SUMMARY RISK ASSESSMENT REPORT

Final report, 2008

Spain

Rapporteur for the risk assessment of 2-nitrotoluene is Spain: Ministry of Environment and Ministry of Health.

Contact points:

Ana Fresno
Ministry of Environment
San Juan de la Cruz s/n
28071-Madrid (Spain)
Fax: +34 91 597 58 16
e-mail: afresno@mma.es

Fernando Carreras Vaquer
Ministry of Health
Paseo del Prado 18-20
28071-Madrid (Spain)
Fax: +34 91 360 13 41
e-mail: sgsasl@msc.es

Working group on Environment:
The scientific work has been prepared by the Department of Environment in the National Institute for Agricultural and Food Research and Technology (INIA) by order of the rapporteur.
Effect assessment: José Vicente Tarazona, Mª Milagrosa Vega and Elena Suárez
Exposure assessment: José Luis Tadeo and Lorena González

Working group on Health: Ministry of Health
Effect assessment: Carmen Barrueco, Covadonga Caballo, Raquel Fernández and Ana Vega
Occupational exposure assessment: Esther Martín

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Final report:	**2008**

PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance 2 nitrotoluene that has been prepared by Spain 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.ec.europa.eu/

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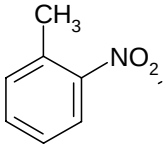
1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS Number: 88-72-2
EINECS Number: 201-853-3
IUPAC Name: 2-nitrotoluene
Synonyms: 1-methyl-2-nitrobenzene
2-methyl-1-nitrobenzene
2-methylnitrobenzene
2-methylnitrobenzol
2-nitro-1-methylbenzol
benzene, 1-methyl-2-nitro
o-methylnitrobenzene
o-nitrotoluene
o-mononitrotoluene
o-nitrotoluol
toluene, *o*-nitro

Molecular weight: 137.14
Molecular formula: $C_7H_7NO_2$
Structural formula:



1.2 PURITY/IMPURITIES, ADDITIVES

Purity: ≥ 99.5%
Impurity 0.2% 3-nitrotoluene
0.01% 4-nitrotoluene

1.3 PHYSICO-CHEMICAL PROPERTIES

Table 1.1: Summary of physico-chemical properties

Property	Value	Comments
Physical state	Liquid	
Melting point	- 9.55 ºC	Kirk-Othmer, 1996
Boiling point	221.7 ºC	Kirk-Othmer, 1996
Relative density	1.16 g/cm^3	at 20 ºC. Verschueren, K., 1996
Vapour pressure	0.028 kPa	at 25 ºC. Hine and Mookerjee, 1975

Table 1.1 continued overleaf

Table 1.1 continued Summary of physico-chemical properties

Water solubility	437 mg/l	at 20 ºC. Bayer AG 2001
Partition coefficient n-octanol/water (log value)	2.3	Hansch & Leo, 1979
Granulometry	Not applicable	n.a.
Conversion factors	n.a.	n.a.
Flash point	95 ºC (DIN 51755)	Bayer AG, 2001
Autoflammability	Ignition temperature: ca. 420 ºC (DIN 51794)	Bayer AG, 2001
Flammability	n.a.	n.a.
Explosive properties	Lower limit : 1.47% by vol Upper limit : 8.8% by vol	Bayer AG, 2001
Oxidizing properties	n.a.	n.a.
Viscosity	2.37 mPa·s	Bayer AG, 2001
Henry's constant	1.2 (Pa.m^3/mol)	Experimental dimensionless Henry´s law constant value proposed by Altschuh, J. *et al.* 1999, transformed into the required units
Surface tension	44.1 mM/m	At 20 ºC; Kirk-Othmer, 1996

1.4 CLASSIFICATION

1.4.1 Current classification

The classification of 2-nitrotoluene in Annex I to Directive 67/548/EEC was revised in the 29th ATP:

Carc. Cat. 2; R45: May cause cancer

Muta. Cat. 2; R46: May cause heritable genetic damage

Repr. Cat. 3; R62: Possible risk of impaired fertility

Xn; R22: Harmful if swallowed

N; R51/53: Toxic to aquatic organisms/May cause long-term adverse effects in the aquatic environment

1.4.2 Proposed classification

It is proposed to keep the same classification as currently:

Carc. Cat. 2; R45: May cause cancer

Muta. Cat. 2; R46: May cause heritable genetic damage

Repr. Cat. 3; R62: Possible risk of impaired fertility

Xn; R22: Harmful if swallowed

N; R51/53: Toxic to aquatic organisms/May cause long-term adverse effects in the aquatic environment.

2 GENERAL INFORMATION ON EXPOSURE

Production

2-nitrotoluene can be produced by either a batch or continuous process in closed systems, by the nitration of toluene. The mononitration of toluene results in the formation of a mixture of the three isomers of nitrotoluene: ortho (2-nitrotoluene), meta (3-nitrotoluene) and para (4-nitrotoluene). If the pure isomer is required, it can be prepared by indirect method, treating 2,4-dinitrotoluene with ammonium sulphide followed by diazotisation and boiling with ethanol.

Estimated production and/or processing amount of 2-nitrotoluene by country is given hereafter in metric tons.

Table 2.1: Production and/or processing volume in metric tons

Site	Volume
A [a]	34,400
B [b]	3,744.56
C [c]	49,200
Total	87,344.56

[a] data from industry, 2000

[b] imported volume. Data from industry, 2003

[c] data from industry, 2002

Uses

The substance is produced and mainly used on-site and in closed systems as an intermediate for further synthesis of *o*-toluidine or 2,4-dinitrotoluene. 2-nitrotoluene can also be used in the synthesis of intermediates for the manufacture of agricultural and rubber chemicals, explosives, heat sensitive colorants, azo and sulphur dyes, and in the organic synthesis of a wide variety of compounds including petrochemicals, pesticides and pharmaceuticals. However, *o*-toluidine seems to be the largest outlet for this substance.

To summarize, data reported by industry of site A about its breakdown of 2-nitrotoluene uses in 2000 indicate that 31,200 tons were used for processing to *o*-toluidine, 500 tons for processing to dinitrotoluene 65/35, 100 tons for processing to 2-nitrotoluene-4-sulfonic acid and 2,600 tons for merchandise. Industry of site B has indicated that 3,698.7 tons of 2-nitrotoluene were converted to *o*-toluidine, via catalytic hydrogenation, in 2003, while 45.86 tons were resold. Finally, information reported by industry of site C indicates that 49,200 tons of 2-nitrotoluene were used as an intermediate for 2,4-dinitrotoluene production in 2002.

Trends

In West Europe, the number of producers of 2-nitrotoluene has decreased in the last years and the use pattern of this compound has changed because 2-nitrotoluene demand has been subject to many fluctuations. In 1991, 2-nitrotoluene was produced by five companies, two in Germany, one in the United Kingdom, one in Sweden and another two in Italy. The Swedish producer was the one that used 2-nitrotoluene for TNT production, but it stopped this production in 1992.

The German producers used 2-nitrotoluene mainly for *o*-toluidine synthesis, though there were some other uses. Nowadays, only one of the German companies continues as 2-nitrotoluene producer and it has increased the capacity for producing *o*-toluidine to cope with higher demand from metolachlor, an herbicide. A mayor part of its production was mainly directed in the past to the production of specialty isocyanates, TDI 65:35 and TDI 100. Increasing competition in the early eighties from other major of these isocyanates, using either the distillation of crude TDI or the 2-nitrotoluene route, forced the industry to reduce its output of these raw materials for polyurethane foams and coatings. The collapse of the demand for TDI 65:35 in Russia since the early nineties had also a severe impact on the demand and pricing of these isocyanates, which no longer provided a good value for 2-nitrotoluene. Therefore, the German producer was pushed to shutdown its isocyanate facility and a large part of 2-nitrotoluene output is preferably converted into o-toluidine since 1985.

Another producer of 2-nitrotoluene in Western Europe, placed in the United Kingdom, had a nitration capacity which was formerly used for the manufacture of nitrochlorobenzenes, but since 1986, 2-nitrotoluene is almost entirely hydrogenated into *o*-toluidine in this site. However, recent information from the industry settled in the United Kingdom shows that its production of 2-nitrotoluene ceased during 2001, although it is still used as a raw material. In 2003, 3,698.7 tons were imported for processing and 45.86 tons were resold.

Table 2.2: Evolution of the quantity of 2-N produced and used in Western Europe in the last 25 years

Year		1978	1983	1985	1987	1991	1992	1996
Production		48,000	50,800	53,500	50,000	52,500	56,000	54,500
Demand	*o*-Toluidine	6,400	17,600	22,200	20,300	31,300	35,500	46,000
	65:35 TDI	24,500	19,500	16,600	17,600	18,400	16,500	-
	TNT	7,000	8,000	10,000	7,000	1,500	2,000	-
	o-Tolidine	1,500	1,500	1,500	1,000	800	-	-
	6-Chloro-2-nitrotoluene	700	800	900	900	600	500	800
	Others	1,000	1,000	1,000	1,000	1,300	1,500	2,000
	Total	41,000	48,400	52,400	47,800	53,900	56,000	48,800

Data from Srour, 1997

In relation to the Italian companies, one had the lowest production in Europe, based on information published in Srour, R., 1997, which was used in the dinitration stream in its TDI facility. But its production stopped in 2003. The other one is nowadays the major producer of 2-nitrotoluene in Europe.

Finally, one conclusion can be put forward: the introduction of metolachlor, in the late seventies increased significantly the demand for *o*-toluidine to a level much higher than any other outlet for this isomer, except for 2,4-dinitrotoluene production, while hardly any 2-nitrotoluene has been offered to TNT producers over the last years (Srour, R.,1997; Industry, 2001).

Legislative controls

In Germany there are several legal regulations related to 2-nitrotoluene:

- Regulations on safeguarding health at the workplace: the maximum workplace concentration is 5 ppm or about 30 mg/m^3 at 20 ºC and 1013 hPa.
- "GesfStoffV" Regulations on Hazardous Substances: 2-nitrotoluene may only be dispensed by a company employee who has proven his or her knowledge and it must be kept under lock and stored so that access is restricted to competent personnel.
- Regulations in German Technical Guidelines for Air Pollution Control: 2-nitrotoluene is assigned to class I, where the mass flow is 0.1 kg/h or more, the mass concentration shall not exceed 20 mg/m^3.
- Regulations for facilities which store, fill or handle water-hazardous substances: 2-nitrotoluene is classified as a water-hazard substance.
- Regulations on combustible fluids: on the basis of its physical properties, 2-nitrotoluene is assigned to class A III.
- Regulations on the transport of hazardous goods: according to the provisions covering the transport of hazardous goods, 2-nitrotoluene is classified as follows:
    - Hazardous Goods Regulations, Railroad: Cl. 6.1, No. 12 b
    - Hazardous Goods Regulations, Road: Cl. 6.1, No. 12 b
    - Hazardous Goods Regulations, Sea: Cl. 6.1, Un No. 1664
    - International regulations on the transportation of dangerous goods by rail / European agreement on the international transportation of dangerous goods by road: Cl. 6.1, No. 12 b
    - International Civil Aviation Organization / International Air Transport Association – Dangerous Goods Regulation (ICAO/IATA-DGR): Cl. 6.1 1664 II
    - Regulations on the transportation of dangerous goods on the Rhine: Cl. 6.1, No. 21 L Cat.

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

Environmental releases

Data on releases from production and processing of 2-nitrotoluene have been reported by industry for all production and/or processing sites. The company of site A, with an air purification unit and an industrial WWTP, reported releases of 25 kg/year to the air and 207 kg/year to water. Regarding site B, where waste waters are discharged to the on-site effluent treatment plant, industry has indicated an annual emission to water lower than 5.5 kg while no information on the value of the emission to air was supplied and therefore, the default factor of 10^{-5} has been considered. Finally, industry of site C indicates an emission to surface water as WWTP effluent of 357 kg/year, over a production period of 11 months. On the other hand, values of total organic content measured in the air emissions are always below 0.5 mg/m^3. Nevertheless, no data on the volume emitted have been supplied and therefore the default factor of 10^{-5} has also been considered to estimate the releases to air.

For regional level, site C has been considered as the worst case for calculations. Finally, the continental emissions will be calculated using the total amount that is produced and used in the EU minus the regional amount.

Table 3.1: Local, regional and continental releases from production and processing (kg•day^{-1})

Compartment	Local			Regional [b]	Continental
	Site A	Site B	Site C		
Air	0.07 [a]	0.125	1.64	1.35	1.05
Waste water	0.57 [a]	0.015 [a]	1.08 [a]	0.978 [a]	0.758

[a] Calculated with emission data provided by industry

[b] Calculated from emission data and production volume of site C as worst case

Regarding the terrestrial compartment, sites A and C indicate that no spreading of sewage sludge from the industrial sewage treatment plants is done. Therefore, the emissions have been calculated only considering atmospheric deposition. Industry from site B indicates that the sludge from the sewage treatment plant is sent off-site for composting prior to spreading on land as an agricultural fertilizer, therefore the spreading of the sludge has been considered as worst case for this site. Finally, no data have been reported by industry related to the emissions to industrial soil, therefore the emission of 1.35 kg/day to industrial soil for regional scale and 1.05 kg/day for continental scale, obtained with EUSES for site C, has been considered as worst case in calculations.

Environmental fate

2-nitrotoluene may be released into the environment during its production and processing. Emissions to water and air are expected to be the most important entry routes of 2-nitrotoluene to the environment.

The available biodegradation data show that 2-nitrotoluene can undergo primary biodegradation to form several products. Ultimate mineralisation to form carbon dioxide or

methane appears to be low over the timeframe of the available studies (>> than 4 weeks). Furthermore on the light of the available information, 2-nitrotoluene should be degraded by biological sewage treatment when suitable acclimation is provided to the cultures, so it can be classified as inherent biodegradable (not readily biodegradable).

The ultimate biodegradation rate constants and half-lives that will be used in the environmental modelling are summarized in Table 3.2.

Table 3.2: Environmental degradation

Compartment		Half life
Atmospheric		23 days
Aquatic	Abiotic degradation	24 days
	Biodegradation	∞ days
Sediment		3,014 days
Soil		300 days

Values utilised in EUSES calculations

Environmental concentrations

Production and processing happen one just after the other in the same place in sites A and C. Therefore, only a PEC_{local} for production and processing is calculated with EUSES for these sites, using the equations given in the TGD. In site B, there is not a production step and consequently only a PEC_{local} for processing has been estimated. In site C, the flow of waste water discharged into a lagoon has been used, and due to the fact that the place is located at a costal zone, the marine exposure has been assessed as well.

Table 3.3 Risk characterisation for surface water

Compartment	Site	Concentration
Surface water	A	$6.58 \cdot 10^{-3}$ µg/l
	B	$1.12 \cdot 10^{-2}$ µg/l
	C	1.66 µg/l
Ground water	A	$6.88 \cdot 10^{-3}$ µg/l
	B	0.195 µg/l
	C	0.145 µg/l
Sewage Treatment Plant	A	$2.49 \cdot 10^{-3}$ mg/l
	B	$3.98 \cdot 10^{-3}$ mg/l
	C	$1.65 \cdot 10^{-2}$ mg/l
Sediment	A	$3.51 \cdot 10^{-2}$ µg/kg wet wt
	B	$5.99 \cdot 10^{-2}$ µg/kg wet wt
	C	8.83 µg/kg wet wt
Sea water	A	0.29 µg/l
Marine sediment	A	1.55 µg/l

Regarding the terrestrial compartment, PECs have been calculated with EUSES for natural soil, agricultural soil and grassland, only considering atmospheric deposition for sites A and C, because industry indicates that there is no spreading of sewage sludge from an industrial

sewage treatment is done. However, industry from site B has indicated that the sludge from the sewage treatment plant is sent off-site for composting prior to spreading on land as an agricultural fertilizer.

Table 3.4: Predicted levels in terrestrial compartment (µg/kg wet wt)

	Site A	Site B	Site C
Soil (total) averaged over 30 days	0.0262	0.903	0.551
Agricultural soil (total) averaged over 180 days	0.0262	0.742	0.551
Grassland (total) averaged over 180 days	0.0434	0.311	0.916

Finally, the annual average PEC_{local} in air has been obtained with EUSES from data of emission reported by industry of site A and it is 0.0167 µg/m^3. Concerning site B no information on the emission to air has been reported, and the estimation of PEC_{local} has been done with default parameters of EUSES, obtaining a value of 0.0285 µg/m^3. Regarding site C, the PEC_{local} obtained using the default factor, as explained above, is 0.375 µg/m^3.

3.2 EFFECTS ASSESSMENT

Aquatic compartment (incl. sediment)

The provided information includes a set of data on the toxicity of 2-nitrotoluene only for fresh water organisms. No information has been provided regarding toxicity on marine organisms. It has not been possible to validate all data going back to the original publications (particularly in relation to fish test), and some values have been included in the assessment when cited in good quality reports. Other non-validated data have been used as additional information to support the assessment produced from the available reports. Values used to establish the proposed PNEC have been checked and validated against the original publications.

There are no data on chronic toxicity to vertebrate aquatic organisms. Anyway, some NOECs (behaviour and mortality) are assessed, after an exposure period of 28 days, by Canton *et al*. (1985). Nevertheless, these endpoints cannot be applied when considering long-term effects.

Invertebrates seem to be the most sensitive taxonomic group, however, the large variation in the acute toxicity effects, even for those results conducted on the same species, i.e. *D. magna*, creates difficulties in comparisons.

A long-term NOEC of 0.5 mg/l on aquatic invertebrates (*Daphnia magna*) has been selected as the lowest value, and used for the $PNEC_{aquatic\ organisms}$ calculation. There are long-term information on aquatic invertebrate and algae, but only short-term information on aquatic vertebrates. Therefore, according to the TGD, an assessment factor of 50 is applied: **$PNEC_{aquatic\ organisms}$** = lowest end chronic toxicity range / 50= 0.5 / 50 = **10 µg/l**.

In rapporteur's opinion, the sound PNEC for the sea water organisms can not be derived appropriately with the available information on fresh water effects. However, following the agreement adopted by the TC NES II 04, a PNEC for marine environment has been derived, according to the Technical Guidance Document, by applying an assessment factor of 500 to the lowest chronic toxicity data on freshwater organisms: **$PNEC_{seawater}$** = lowest chronic freshwater toxicity / 500= 0.5 / 500 = **1 µg/l**.

The only available Data Set information on sediment organisms includes a single datum on the effect of 2-nitrotoluene on Tubifex sp. The EC50 obtained for this organism is much more higher than the other for the aquatic invertebrates. For the oligochaeta Tubifex sp., 2-nitrotoluene has shown a 24-h LC50 of 410 mg/l and 48-h LC50 of 370 mg/l (these results must be considered under the light of the fact that the mortality in the control was above 10%) (Yoshioka et al., 1986b). (It was no possible to validate this information, since only the abstract was provided in English, and so, even the exposure route could not be determined appropriately). No data have been provided regarding toxicity on marine sediment organisms.

No relevant sediment toxicity information has been provided. So, taking into account the physical-chemical properties of the substance, the equilibrium partitioning method is considered to be appropriate for the $PNEC_{sediment}$ derivation. The PNEC for sediment is calculated according to the Technical Guidance Document. Where: $K_{susp\text{-}water}$ = suspended sediment-water coefficient = 6.14 m^3/m^3 for 2-nitrotoluene; RHO_{susp} = bulk density of suspended sediment = 1150 kg/m^3. **$PNEC_{sed}$** = 6.14 m^3/m^3 x 10 µg/l x 1000 / 1150 kg/m^3 = **53.4 µg/kg ww**.

Following the same approach, and using the equilibrium partitioning method, the PNEC for the marine sediment will be: **$PNEC_{marine\text{-}sediment}$** = 6.14 m^3/m^3 x 1 µg/l x 1000 / 1150 kg/m^3 = **5.34 µg/kg ww**.

A validated EC_{50} value of 665 mg/l, obtained according to the OECD guideline 209, has been used for calculations, to which it would be applied a factor of 100. **$PNEC_{microorganisms}$** = respiration / 100= 665 / 100 = **6.65 mg/l**.

It has not been possible to check and validate the information regarding the lowest fermentation data (NOEC = 60 mg/l) provided by Hoechst (1984), which was included in the IUCLID database. Assuming that this value may be correct, and applying an assessment factor of 10 as recommend for a NOEC, a PNEC of 6 mg/l should be proposed. Taking into account that the former PNEC, derived from the effects on respiration (6.65 mg/l), is very similar to the PNEC obtained from the NOEC on fermentation, there is no need for requesting formally the fermentation study as no differences in the PNEC are expected. The calculated PNEC is lower than the toxicity threshold values provided for the different protozoa, and therefore, the proposed PNEC is considered to be protective for the role of these organisms in WWTP.

Terrestrial compartment

Regarding the terrestrial compartment, no toxicological information has been provided.

Taken into account the lack of data, and according to the Technical Guidance Document, the equilibrium partitioning method can be applied as a conservative calculation method to identify a potential risk to the soil compartment. Thus, the PNEC has been calculated using the equilibrium partitioning method with the PNEC for aquatic organisms. Where: $K_{soil\text{-}water}$ = soil-water partition coefficient = 6.48 m^3/m^3 for 2-nitrotoluene; RHO_{soil} = bulk density of wet soil = 1700 kg/m^3; **$PNEC_{soil}$** = 6.48 m^3/m^3 x 10 µg/l x 1000 / 1700 kg/m^3 = **38.11 µg/kg**.

Considering the PNEC for microorganisms, it can be assumed that the equilibrium partitioning method would protect also the soil microbial community from undesirable effects. But there is no information in relation to the possibility of covering also the effects on vascular plants.

Atmosphere

No information is available on the effects of 2-nitrotoluene to plants and other organisms exposed via air, although volatilisation to the atmosphere may be likely to be limited due to the vapour pressure of the substance.

Secondary poisoning

According to the low bioaccumulation potential and the rapid elimination of this compound in fish and mammals, no secondary poisoning potential is expected from this substance.

3.3 RISK CHARACTERISATION

Aquatic compartment (incl. sediment)

Local, regional and continental PECs for aquatic and sediment compartments have been compared to a $PNEC_{aquatic}$ of 10 µg/l and a $PNEC_{seawater}$ of 1 µg/l, derived from available information. And a $PNEC_{sediment}$ of 53.4 µg/kg ww and a $PNEC_{marine\_sediment}$ of 5.34 µg/kg ww, calculated using the equilibrium partitioning method according to the TGD. For the assessment of the Sewage Treatment Plants, a $PNEC_{microorganisms}$ of 6.65 mg/l, will be used.

Table 3.5: Risk characterisation for surface water

Local compartment	Site	$PEC/PNEC_{surface\ water}$ (µg/l)	$PEC/PNEC_{sea\ water}$ (µg/l)	$PEC/PNEC_{STP}$ (mg/l)	$PEC/PNEC_{sediment}$ (µg/kg ww)	$PEC/PNEC_{marine\ sediment}$ (µg/kg ww)
	A	$6.58 \cdot 10^{-4}$		$3.74 \cdot 10^{-4}$	$6.57 \cdot 10^{-4}$	
	B	$1.12 \cdot 10^{-3}$		$5.98 \cdot 10^{-4}$	$1.12 \cdot 10^{-3}$	
	C	0.166	0.29	$2.48 \cdot 10^{-3}$	0.16	0.29
Regional Compartment		PEC/PNEC				
Surface water (total) (µg/l)		$3.39 \cdot 10^{-4}$				
Surface water (dissolved) (µg/l)		$3.39 \cdot 10^{-4}$				
Sediment (total) (µg/kg wet wt)		$3.24 \cdot 10^{-4}$				
Continental Compartment		PEC/PNEC				
Surface water (total) (µg/l)		$4.42 \cdot 10^{-6}$				
Surface water (dissolved) (µg/l)		$4.42 \cdot 10^{-6}$				
Sediment (total) (µg/kg wet wt)		$4.45 \cdot 10^{-6}$				

Conclusions to the risk assessment for the aquatic compartment:

Conclusion (ii) applies to the aquatic compartment.

Terrestrial compartment

Local, regional and continental PECs for the terrestrial compartment have been compared to the $PNEC_{soil}$ of 38.11 µg/kg, calculated using the equilibrium partitioning method according to the TGD.

Table 3.6: Predicted levels in terrestrial compartment

Local Compartment	Site	PEC/PNEC
Soil (total) averaged over 30 days (µg/kg wet wt)	A	$6.87 \cdot 10^{-4}$
	B	0.023
	C	0.014
Agricultural soil (total) averaged over 180 days (µg/kg wet wt)	A	$6.87 \cdot 10^{-4}$
	B	0.0194
	C	0.014
Grassland (total) averaged over 180 days (µg/kg wet wt)	A	$1.13 \cdot 10^{-3}$
	B	$8.16 \cdot 10^{-3}$
	C	0.024
Regional Compartment		**PEC/PNEC**
Agricultural soil (total) (µg/kg wet wt)		$5.16 \cdot 10^{-5}$
Natural soil (total) (µg/kg wet wt)		$7.53 \cdot 10^{-6}$
Industrial soil (total) (µg/kg wet wt)		0.016
Continental Compartment		**PEC/PNEC**
Agricultural soil (total) (µg/kg wet wt)		$9.10 \cdot 10^{-7}$
Natural soil (total) (µg/kg wet wt)		$1.03 \cdot 10^{-6}$
Industrial soil (total) (µg/kg wet wt)		$1.5 \cdot 10^{-4}$

Conclusions to the risk assessment for the terrestrial compartment:

Conclusion (**ii)** applies to the terrestrial compartment.

Atmosphere

No effects on the atmosphere are likely in the regional and continental scenarios, because of the low predicted environmental concentrations of 2-nitrotoluene.

Table 3.7: Predicted levels in air compartment

Scale		PEC (µg/m^3)
Local	Site A	0.0167
	Site B	0.0285
	Site C	0.375
Regional		$3.39 \cdot 10^{-3}$
Continental		$4.42 \cdot 10^{-5}$

Nevertheless, a preliminary assessment can be done using data from the Human Health Assessment. Several values regarding inhalation toxicity could be used: the NOAEC value of 1086 mg/m^3 derived from an acute 8-hour inhalatory toxicity study in rats as a starting point, the corresponding human NAEC of 727.62 mg/m^3,and the LAEC of 175 mg/m^3 derived from an oral LOAEL of 25 mg/kg bw in rats for repeated dose toxicity. Among them, the lowest concentration, 175 mg/m^3, has been compared with the highest PEC_{local}, 0.375 µg/m^3, and the ratio obtained is $466 \cdot 10^3$, which indicates a low concern for inhalation exposure.

Conclusions to the risk assessment for the atmosphere:

Conclusion (ii) applies to atmospheric compartment.

Secondary poisoning

According to the low bioaccumulation potential and the rapid elimination of this compound in fish and mammals, no secondary poisoning potential is expected from this substance.

Conclusions to the risk assessment for secondary poisoning:

Conclusion (**ii)** applies to the secondary poisoning.

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

Occupational exposure

2-nitrotoluene is a yellow liquid at room temperature with a vapour pressure of 0.16 hPa at 20ºC.

The substance is produced and used in closed systems as an intermediate for further synthesis. Once manufactured it is mainly used on site as a intermediate in the synthesis of *o*-toluidine or as a non isolated intermediate in the synthesis of dinitrotoluene. The manufacture of *o*-toluidine accounts for nearly 90% of total 2-nitrotoluene consumption in Europe.

Given the high captive consumption of this substance, one scenario is only considered.

Exposure may occur during activities that involve breaching the closed system such as sampling or loading and unloading of tanks and drums.

Measured exposure data of limited quality is available. A reasonable worst-case full shift exposure level of 0.3 mg/m^3 is estimated based on the highest exposure value for the whole shift and the result of EASE model. Typical values can be considered in the order of 0.1 mg/m^3. A reasonable worst-case short term value of twice as high as the full shift value is assumed: up to 0.6 mg/m^3.

Dermal exposure is considered highest for the activity of filling and emptying drums. The reasonable worst-case exposure estimated by EASE model is 420 mg/day. The assessment has been carried out without taking into account the use of PPE. When PPE is used in accordance with Directive 89/656/EEC (this is, in fact, obligatory around the EU), dermal exposure will be considerably reduced.

Consumer exposure

2-nitrotoluene can be used in the chemical industry in the synthesis of intermediates for azo dyes, sulfur dyes, rubber chemicals, and agriculture chemicals. There is not information about 2-nitrotoluene in consumer products. However, given the intended use, the exposure of consumers to the substance is expected to be negligible.

Humans exposed via the environment

Indirect exposure via the environment is calculated using data for oral intake via food, drinking water and air for local (A, B and C sites) and regional scales. The resultant daily doses, for the uptake of 2-nitrotoluene, are in the table below:

Table 4.1: Daily Human Doses ($mg \cdot kg^{-1} \cdot d^{-1}$)

Intake route	Site A (Germany)	Site B (United Kingdom)	Site C (Italy)	Regional
Drinking water	$1.96 \cdot 10^{-7}$	$5.56 \cdot 10^{-6}$	$3.89 \cdot 10^{-5}$	$9.67 \cdot 10^{-8}$
Fish	$1.76 \cdot 10^{-7}$	$2.89 \cdot 10^{-7}$	$4.02 \cdot 10^{-5}$	$1 \cdot 10^{-7}$
Leaf crops	$1.69 \cdot 10^{-6}$	$3.04 \cdot 10^{-6}$	$3.95 \cdot 10^{-5}$	$3.72 \cdot 10^{-9}$
Root crops	$1.18 \cdot 10^{-7}$	$3.33 \cdot 10^{-6}$	$2.47 \cdot 10^{-6}$	$8.82 \cdot 10^{-9}$
Meat	$1.94 \cdot 10^{-10}$	$5.66 \cdot 10^{-10}$	$5.97 \cdot 10^{-9}$	$4.44 \cdot 10^{-12}$
Milk	$5.74 \cdot 10^{-9}$	$1.67 \cdot 10^{-9}$	$1.76 \cdot 10^{-8}$	$1.31 \cdot 10^{-11}$
Air	$3.43 \cdot 10^{-6}$	$6.12 \cdot 10^{-6}$	$8.03 \cdot 10^{-5}$	$7.39 \cdot 10^{-9}$
Total	$5.63 \cdot 10^{-6}$	$1.84 \cdot 10^{-5}$	$2.01 \cdot 10^{-4}$	$2.17 \cdot 10^{-7}$

Combined exposure

Exposure to 2-nitrotoluene may reasonably be predicted to arise as a result of combined exposure from workplace and environmental sources.

4.1.2 Effects assessment

There are not available data on toxicokinetics of 2-nitrotoluene in humans but several studies following oral administration have been performed in experimental animals, especially in rats. *In vitro* studies provide additional information on the metabolism.

In rats, 2-nitrotoluene is rapidly absorbed, extensively metabolised and rapidly excreted. Its half-life in plasma was about 1.5 hours. Oral absorption was determined to be 100% within 24 hours based on excretion of radioactivity (more than 95% in urine from both sexes) obtained after a single oral dose of 2 mg/kg b.w. There were no differences between sexes. In addition, similar results were obtained in rats administered a single or a repeated oral dose of 200 mg/kg b.w.

Oral absorption in male mice was determined to be 100% within 72 hours based on excretion of radioactivity (85% in the urine) obtained after a single oral dose of 2 mg/kg b.w. Similar results were obtained in mice administered a single oral dose of 200 mg/kg b.w.

No data are available for inhalation exposure route. Then, the worst case inhalation absorption should be assumed (i.e. 100%).

No data are available for dermal exposure route. Then, a default value for dermal absorption of 100% should be applicable based on both the physico-chemical properties of the substance (MW= 137.14, log P_{ow}= 2.3) and the oral excretion data.

Pertinent data were not located on distribution. However, 2-nitrotoluene appears to be well distributed as indicated by toxicity in various organs of rats or mice orally exposed. In rats, toxicity was observed mainly in liver, kidney, spleen, testes and haematopoietic system. In addition, based on excretion data (a total recovery of radioactivity in urine and faeces of rats and mice 24 or 72 hours after dosing) it is appropriate to state “no evidence of accumulation”.

No parent compound was detected in urinary samples of rodents. In rats, at least nine urinary metabolites were identified, four major: 2-nitrobenzoic acid, 2-nitrobenzyl glucuronide, 2-

aminobenzyl alcohol and S-(2-nitrobenzyl)-N-acetylcysteine, and five minor: S-(2-nitrobenzyl)-glutathione, 2-nitrobenzyl sulfate, 2-nitrobenzyl alcohol, 2-aminobenzoic acid and *o*-toluidine. The metabolite profiles after single (using two dose levels) and repeated doses were similar; there was a sex-dependent variance in metabolite profile with females excreting significantly less 2-aminobenzyl alcohol and S-(2-nitrobenzyl)-N-acetylcysteine than males, but more 2-nitrobenzoic acid. In mice, only two major metabolites, 2-nitrobenzoic acid and 2-nitrobenzyl glucuronide, were identified in urine.

The major metabolite excreted in bile of rats following 2-nitrotoluene administration was 2-nitrobenzyl glucuronide. Males excreted about 3 times as much of this metabolite as did females.

The metabolism of 2-nitrotoluene proceeds firstly by cytochrome-P450 mediated oxidation to nitrobenzyl alcohol which then undergoes metabolism by four pathways: a) oxidation to 2-nitrobenzoic acid; b) conjugation with glutathione to 2-nitrobenzylmercapturic acid; c) nitro-group reduction to 2-aminobenzoic acid; and d) conjugation with glucuronic acid to 2-nitrobenzyl glucuronide. This latter pathway appears as the responsible of 2-nitrotoluene bioactivation. The glucuronide metabolite secreted in the bile is believed to be converted to 2-aminobenzyl alcohol by hydrolytic and reductive activities of intestinal microflora, and then systemically reabsorbed. The final activation step is dependent upon sulfotransferase. Two enzyme-mediated pathways are involved. One of them requires *in vitro* PAPS (3'-phosphoadenosine 5'-phosphosulfate) and cytosolic enzymes and generates a compound (likely, 2-aminobenzyl sulfate) that binds covalently to DNA. The reactivity of 2-aminobenzyl sulfate with DNA could be related to the ease formation of a reactive benzyl cation due to electrondonating ability of the amino group. The other pathway requires *in vitro* hepatic microsomal enzymes and NADPH and results in an intermediate that binds covalently to protein. There is evidence that oxidation of 2-aminobenzyl to 2-(N-hydroxylamino) benzyl alcohol followed by sulfation yields an unstable N-sulphate which decomposes to an electrophilic nitrenium and/or carbonium ions. Since *o*-nitrotoluene, but not *m*- or *p*-nitrotoluene, induced DNA repair in the *in vivo* UDS assay in male rats, the *syn* conformation of DNA adducts appears to be a determinant factor in the genotoxic response.

The routes of excretion were similar in rats and mice, with the predominant route being via urine. By 72 hours after a single oral dose of 2 mg/kg b.w., the percentages of the radioactivity recovered in the urine were 100% (rats) and 85% (mice), and faecal excretion accounted for 4-5% (rats), and 23% (male mice). Minimal amounts of radiolabel (0.1%) were captured in expired air. The rate of excretion was more rapid in rats, with about 100% of the radioactivity excreted in urine in the first 24 hours. Less than 70% of the administered radioactivity was excreted in urine by mice in the same time period.

For male and female rats similarly treated, biliary excretion measured after 12 h was greater for males (29%) than for females (10%). Since proportionately less label is excreted via the faeces it is presumed that the label is reabsorbed from the gut. In addition, cannulation of the bile duct inhibits covalent binding in the liver indicating the involvement of the enterohepatic circulation.

There are available information on the effects of exposure to 2-nitrotoluene in humans but data on acute toxicity are limited to inhalation exposure. The usefulness of these data is limited because the exposure duration was not reported and consequently a NOAEC/LOAEC could not be determined. Therefore information on acute toxicity has been derived from animal data. The available studies on both inhalation and dermal acute toxicity have limited quality especially with respect to the identity of the test substance (purity not reported).

However, as results from such a batch of studies are consistent, they can, together, provided sufficient information on the acute toxicity of the substance. At saturated vapour concentrations, 190.8 ppm (1.086 mg/L) for 8 h or 320 ppm (1.795 mg/L) for 4 h in rats and 354 ppm (1.986 mg/L) for 4 h in mice, 2-nitrotoluene, did not produce mortalities, toxicity and gross lesions within 14-day observation period. In a limit test, 2-nitrotoluene (5000 mg/kg b.w. in rats and 20000 mg/kg b.w. in rabbits) did not produce either mortality or toxicity within 14-day observation period. Therefore, according to EU criteria, no classification is necessary for acute toxicity following either inhalation or dermal exposure. The available studies on acute oral toxicity have limited quality (only in one study purity was reported). However, as results from such a batch of studies are consistent, they can, together, provided sufficient information on the acute toxicity of the substance. The oral LD_{50} value ranged from 890 to 2546 mg/kg b.w. in rats, from 970 to 2462 mg/kg b.w. in mice and was determined to be 1750 mg/kg b.w in rabbit. Clinical signs of toxicity were related with methaemoglobin formation. Based on the lower oral LD_{50} value (890 mg/kg b.w in rats), according to EU criteria, 2-nitrotoluene is classified as Xn; R22.

The weight of evidence from good quality animal studies indicates that 2-nitrotoluene is not either irritant or corrosive for the skin and eyes. In relation to the respiratory tract, the acute inhalation toxicity studies in rodents have not revealed any signs of irritation. However, an olfactory degeneration was observed in both sub-chronic toxicity and carcinogenicity dietary studies in mice, and did not occur in rats. This effect was not seen with the other isomers, which have the same volatility. Accordingly, the olfactory degeneration is considered a mouse specific systemic effect. Therefore, the classification for respiratory tract irritation is not justified.

There are no data on skin or respiratory sensitisation to 2-nitrotoluene in animals or in humans. However, it is considered significant the absence of positive reports on such effects in humans.

There were not available data in humans and neither in experimental animals following inhalation or dermal exposure but several studies have been investigated the toxicity of 2-nitrotoluene following repeated oral administration to rats and mice. Most of feed studies were performed in essence according to OECD guidelines and in conformity with GLP. Rat was the most susceptible species of the ones tested for repeated dose toxicity of 2-nitrotoluene. In the 14-day studies, 2-nitrotoluene, administered up to 5000 ppm (mice) or 10000 ppm (rats), did not cause either effects on survival or clinical signs of toxicity, although 5000 ppm animals showed decreases in body weight gains relative to controls. In addition, a minimal oval cell hyperplasia in liver was observed only in 10000 ppm male rats. Therefore, 10000 ppm was selected the high concentration for 13-week studies. At the 13-week toxicity studies, relative liver weights were increased from 625 ppm in both sexes of rats. However, at this dose level there was not treatment-related histopathology. Non-neoplastic lesions occurred at dose levels of 1250 ppm and above. Therefore, the NOAEL for subchronic-toxicity was considered to be 625 ppm (45 mg/kg b.w.) based on capsular fibrosis observed in spleen of male rats at 1250 ppm (89 mg/kg b.w.). In mice, the only histopathological lesion observed was degeneration and metaplasia of the olfactory epithelium in both sexes from 1250 ppm (223 and 268 mg/kg b.w. for males and females, respectively). At the two-year carcinogenicity study, non-neoplastic lesions occurred at the lower dose level tested of 625 ppm in rats and 1250 ppm in mice. Therefore, the LOAEL for chronic toxicity was considered to be 625 ppm in rats (25 and 30 mg/kg b.w. in males and females, respectively) based on lesions observed in liver, bone marrow, spleen and lung for both sexes and in mammary gland and mandibular lymph node only for females.

Most of the *in vitro* genotoxicity tests carried out with 2-nitrotoluene were negative. However, 2-nitrotoluene was an *in vivo* genotoxic agent for somatic cells. Positive results were found in the UDS test for both male and female rats. Males were more sensitive to genotoxicity of 2-nitrotoluene. A sex difference in biliary excretion may explain the sex difference in the genotoxicity of 2-nitrotoluene. In addition, 2-nitrotoluene did not induce DNA repair in germ-free animals, whereas DNA repair was induced in Charles River Altered Schaedler Flora-associated animals. Male and female F344 rats were shown to have similar populations of intestinal bacteria; however at the doses used, females were resistant to the genotoxic action of 2-NT. These results indicate the obligatory role of intestinal bacteria in the metabolic activation of 2-nitrotoluene, showing that the genotoxic potential of 2-nitrotoluene is dependent upon the sex of the animal under study. On the other hand, gene mutations in *ras, p53* and *β-catenin* genes were observed in hemangiosarcomas from $B6C3F_1$ mice exposed to 2-nitrotoluene in feed for 2 years, but not in spontaneous hemangiosarcomas. These *in vivo* data suggest 2-nitrotoluene is metabolized to mutagenic intermediates and that could be the reason why most of the *in vitro* genotoxicity tests were negative. In conclusion, 2-nitrotoluene is mutagenic in somatic cells, and it reaches the germ cells since toxicity was observed in testis and epididymis of rats. Therefore, according to the TGD (2005) criteria the classification of 2-nitrotoluene as mutagenic category 2 (T; R46) is justified.

No 2-nitrotoluene epidemiology studies on carcinogenesis have been reported in the literature. However, excess cancers have been found in workers exposed to a related chemical, *o*-toluidine. Only a long-term feed carcinogenicity study in rodents is available, performed in essence according to OECD guideline 451 and GLP compliant. There was clear evidence of carcinogenic activity of 2-nitrotoluene in rats, based on increased incidences of malignant mesothelioma, subcutaneous skin neoplasms, mammary gland fibroadenoma and liver neoplasms in males and increased incidences of subcutaneous skin neoplasms and mammary gland fibroadenoma in females. The increased incidences of lung neoplasms in males and of hepatocellular adenoma in females were also considered to be exposure related. Malignant mesotheliomas occurred with incidences of 33%, 48% and 73% in the 625, 1250 and 2000 ppm core study male rat groups, respectively. The incidences of malignant mesotheliomas were 73% and 90% in the 2000 and 5000 ppm stop-exposure male rat groups. The incidence of mesothelioma was higher in the 2000 stop-exposure group than in the 625 ppm even though the latter group received approximately 50% more total exposure to 2-nitrotoluene. The incidences of mesotheliomas were similar in the 2000 ppm core study and stop-exposure groups of male rats. Thus, critical events leading to mesothelioma occurred early in the study, and this damage was irreversible. There was clear evidence of carcinogenic activity of 2-nitrotoluene in male and female mice based on increased incidences of hemangiosarcoma, carcinoma of the large intestine (cecum), and hepatocellular neoplasms (females only because males died early due to the development of hemangiosarcomas). The occurrence of *p53* or β–catenin mutations in 2-nitrotoluene-induced hemangiosarcomas, but not in spontaneous hemangiosarcomas, suggest that the pathways leading to 2-nitrotoluene-induced cancer differ from the pathways in spontaneous hemangiosarcomas. In summary, there is a good evidence of an increase in tumour incidence at multiple sites in both rats and mice. There is also evidence that time to onset is very short. These observations are consistent with genotoxic aetiology, which is consistent with the findings from the genotoxicity studies. Therefore, according to EU criteria, 2-nitrotoluene is considered carcinogenic category 2 and then classified as T; R45.

There are no data on toxicity for reproduction in humans. The only animal data are derived from non-standard reproduction studies. In rats, 2-nitrotoluene administered in feed at 5000 ppm for 13 weeks causes damage to the testes and the epididymis with a simultaneous

reduction in the sperm count and the motility of the sperm in males, and a prolongation of the menstrual cycle among the females. Reduced sperm motility was also observed at 10000 ppm (the highest dose level tested) for the mouse. The NOAEL for impair fertility was considered to be 2500 ppm (179 mg/kg bw) in male rats. The testicular effects indicate a need for fertility classification but because they occur at toxic dose levels, while clear-cut effects on fertility seem absent, indeed only toxic for reproduction category 3 (Xn; R62) is justified according to EU criteria. With respect to the development, in a study where male and female CD rats received 2-nitrotoluene at daily doses of 0, 50, 150 or 450 mg/kg/d over a total period of approximately 10 weeks, the only effect considered as indicative of developmental toxicity was the retardation in pup growth. The LOAEL was considered to be 50 mg/kg/d. However, because of the absence of further details on its severity, this effect cannot be used for classification. In addition, it cannot be ruled out that some toxicity is due to the transfer of the substance through the milk. This effect was not observed in another Wistar rat study. Differences on results between studies could be due to differences on sensitivity between strains. Therefore, based on available data and the EU criteria, the classification for developmental toxicity is not justified.

4.1.3 Risk characterisation

4.1.3.1 Human health (toxicological properties)

Workers

When considering the risks to human health arising from occupational exposure to 2-nitrotoluene, the key areas of concern are for mutagenicity and carcinogenicity.

Overall, the available data do not allow the identification of a threshold level of exposure below which there would be no risk for the development of these effects in humans. In view of this, there are potential health concerns at all exposure levels. According to the quantitative risk characterization by concerns for carcinogenicity, the exposure scenario life-time cancer risk for workers by both inhalation and dermal routes is clearly greater than the established default cancer risk value. The same quantitative risk characterization was applied for somatic and germ cell mutagenicity. Therefore, conclusion (iii) is reached for both carcinogenicity and mutagenicity as a consequence of inhalation and dermal exposure.

In relation to sensitization, **conclusion (i) "on hold"** is proposed for skin sensitization, assuming that the knowledge that the substance be a skin sensitiser would not lead to stricter control measures than need to be applied for a genotoxic carcinogen.

In addition, regarding repeated dose toxicity and toxicity for reproduction (fertility and development), the calculated MOS are judged not to be enough for workers exposed by dermal route. Although high standards of control are assumed for these industry sectors representing best practice, there is no evidence that these standards are applied across EU industry. Thus, there is no evidence that the appropriate equipment is in place in work places and that it is used and maintained in the correct manner. Therefore, **conclusion (iii)** is reached for both repeated dose toxicity and toxicity for reproduction (fertility and development) as a consequence of dermal exposure.
On the other hand, there is no concern for the remaining end-points: acute toxicity by inhalation and dermal route; irritation/corrosivity to skin, eye or the respiratory tract; repeated

dose toxicity by inhalation; and toxicity for reproduction (fertility and development) by inhalation. Therefore, **conclusion (ii)** applies.

Consumers

Exposure of the consumers is not assumed to exist. Therefore, **conclusion (ii)** is reached.

Humans exposed via the environment

When considering the risks to human health arising from indirect exposure to 2-nitrotoluene via environment the key areas of concern are for mutagenicity and carcinogenicity.

Overall, the available data do not allow the identification of a threshold level of exposure below which there would be no risk for the development of these effects in humans. In view of this, there are potential health concerns at all exposure levels. According to the quantitative risk characterization for carcinogenicity, the local site C is considered the only scenario of concern; the remaining sites are of very low concern. The same quantitative risk characterization was applied for somatic and germ cell mutagenicity. Therefore, **conclusion (iii)** is reached for both carcinogenicity and mutagenicity as a consequence of inhalation and oral exposure arising from the local site C.

The calculated MOS for total exposure (oral and inhalation routes) of man via the environment in both local and regional scales are judged to be enough regarding repeated dose toxicity and toxicity for reproduction (fertility and development) and **conclusion (ii)** is reached.

Combined exposure

Exposure to 2-nitrotoluene may reasonably be predicted to arise as a result of combined exposure from workplace and environmental sources. The risk to human health under conditions of combined exposure is dominated by occupational exposure.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

There is not risk of concern in the industry setting, regarding its physico-chemical properties. Adequate safety measures are taken and information is provided on the label and safety data sheet. Therefore, since risk reduction measures already being applied are considered sufficient, **conclusion (ii)** is reached.

5 RESULTS

5.1 ENVIRONMENT

Aquatic compartment (incl. sediment)

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

This conclusion applies to the aquatic compartment.

Terrestrial compartment

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

This conclusion applies to the terrestrial compartment.

Atmosphere

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

This conclusion applies to the atmospheric compartment.

Secondary poisoning

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

This conclusion applies to the secondary poisoning.

5.2 HUMAN HEALTH

5.2.1 Human health (toxicity)

Workers

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

This conclusion is reached because of:

concerns for carcinogenicity and mutagenicity as a consequence of inhalation and dermal exposure.

concerns for repeated dose toxicity and toxicity for reproduction (fertility and development) as a consequence of dermal exposure.

Conclusion (i) "on hold" There is need for further information and/or testing

This conclusion is proposed for skin sensitization, assuming that the knowledge that the substance be a skin sensitiser would not lead to stricter control measures than need to be applied for a genotoxic carcinogen

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

This conclusion is reached for acute toxicity by inhalation and dermal routes; irritation/corrosivity to skin, eye or the respiratory tract; repeated dose toxicity by inhalation; and toxicity for reproduction (fertility and development) by inhalation, because these endpoints are of no concern.

Consumers

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

This conclusion is reached because exposure of consumers is not assumed to exist.

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:

- concerns for carcinogenicity and mutagenicity as a consequence of inhalation and oral exposure arising from the local site C**.**

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

This conclusion is reached for repeated dose toxicity and toxicity for reproduction (fertility and development) because the calculated MOS for total exposure (oral and inhalation routes) of man via the environment in both local and regional scales are judged to be enough for these endpoints.

Combined exposure

The risk to human health under conditions of combined exposure is dominated by occupational exposure.

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 no need for risk reduction measures beyond those which are being applied already.

This conclusion is reached because the risk assessment shows that risks are not expected, and risk reduction measures already being applied are considered sufficient.

European Commission

EUR 23517 EN/2 **European Union Summary Risk Assessment Report**
2-Nitrotoluene

Editors: S. Pakalin, K. Aschberger, A. Paya-Perez, G. Urselli, S. Vegro.

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The report provides the summary of the comprehensive risk assessment of the substance 2-nitrotoluene It has been prepared by Spain in the frame of Council Regulation (EEC) No. 793/93 on the evaluation and control of the risks of existing substances, following the principles for assessment of the risks to man and the environment, laid down in Commission Regulation (EC) No. 1488/94.

Part I - Environment
This part of the evaluation considers the emissions and the resulting exposure to the environment in all life cycle steps. Following the exposure assessment, the environmental risk characterisation for each protection goal in the aquatic, terrestrial and atmospheric compartment has been determined.

The environmental risk assessment concludes that there is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Part II – Human Health
This part of the evaluation considers the emissions and the resulting exposure to human populations in all life cycle steps. The scenarios for occupational exposure, consumer exposure and humans exposed via the environment have been examined and the possible risks have been identified.

The human health risk assessment concludes that there is concern for workers with regard to mutagenicity and carcinogenicity as a consequence of inhalation and dermal exposure and with regard to repeated dose toxicity and toxicity for reproduction (fertilty and development) as a consequence of dermal exposure. There is also concern for humans exposed via the environment with regard to carcinogenicity and mutagenicity as a consequence of inhalation and oral exposure arising from one and all local sites respectively. For consumers and for human health (physico-chemical properties) there is no concern.

The conclusions of this report will lead to risk reduction measures to be proposed by the Commission's committee on risk reduction strategies set up in support of Council Regulation (EEC) N. 793/93.