

Annex XV report

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE OF VERY HIGH CONCERN ON THE BASIS OF THE CRITERIA SET OUT IN REACH ARTICLE 57

Substance Name: Nitrobenzene

EC Number: 202-716-0

CAS Number: 98-95-3

Submitted by: Environment Agency Austria on behalf of the Austrian Competent Authority (Austrian Federal Ministry of Agriculture, Forestry, Environment and Water Management)

Date: August 25th 2015

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PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE OF VERY HIGH CONCERN ON THE BASIS OF THE CRITERIA SET OUT IN REACH ARTICLE 57

Substance Name(s): Nitrobenzene

EC Number(s): 202-716-0

CAS number(s): 98-95-3

- The substance is proposed to be identified as a substance meeting the criteria of Article 57 (c) of Regulation (EC) No 1907/2006 (REACH) owing to its classification in the hazard class reproductive toxicity category 1B (H360F 'May damage fertility').

Summary of how the substance meets the criteria set out in Article 57 of the REACH Regulation

Nitrobenzene is covered by index number 609-003-00-7 of Regulation (EC) No 1272/2008 in Annex VI, part 3, Table 3.1 (the list of harmonised classification and labelling of hazardous substances) and it is classified in the hazard class reproductive toxicity category 1B (H360F 'May damage fertility').

Therefore, this classification of the substance in Regulation (EC) No 1272/2008 shows that it meets the criteria for classification in the hazard class:

- Reproductive toxicity category 1B in accordance with Article 57 (c) of REACH.

Registration dossiers submitted for the substance? Yes

PART I

Justification

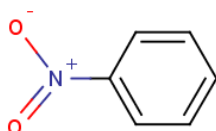
1. Identity of the substance and physical and chemical properties

1.1. Name and other identifiers of the substance

Table 1: Substance identity

EC number:	202-716-0
EC name:	nitrobenzene
CAS number (in the EC inventory):	98-95-3
CAS number: Deleted CAS numbers:	98-95-3
CAS name:	Benzene, nitro-
IUPAC name:	nitrobenzene
Index number in Annex VI of the CLP Regulation	609-003-00-7
Molecular formula:	C ₆ H ₅ NO ₂
Molecular weight range:	123.11
Synonyms:	<i>Nitrobenzol, mirbane oil, essence of mirbane, p-Nitrobenzene, Mononitrobenzene</i>

Structural formula:



1.2. Composition of the substance

Name: Nitrobenzene

Description: colourless to yellow, oily liquid with a pungent odour.

Substance type: mono-constituent

Table 2: Constituents

Constituents	Typical concentration	Concentration range	Remarks
Nitrobenzene EC 202-716-0	≥80 - 100% (w/w)	≥80 - 100% (w/w)	

1.3. Identity and composition of degradation products/metabolites relevant for the SVHC assessment

Not relevant for the identification of the substance as SVHC in accordance with Article 57 points (a) to (c).

1.4. Identity and composition of structurally related substances (used in a grouping or read-across approach)

Not relevant for the identification of the substance as SVHC in accordance with Article 57 points (a) to (c).

1.5. Physicochemical properties

Not relevant for the identification of the substance as SVHC in accordance with Article 57 points (a) to (c).

2. Harmonised classification and labelling

Nitrobenzene is covered by Index number 609-003-00-7 in part 3 of Annex VI to the CLP Regulation as follows:

Table 3: Classification according to Annex VI, Table 3.1 (list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008 amended by 944/2013/EC (5th ATP).

Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Spec. Conc. Limits, M-factors	Notes
				Hazard Class and Category Code(s)	Hazard statement code(s)	Pictogram, Signal Word Code(s)	Hazard statement code(s)	Suppl. Hazard statement code(s)		
609-003-00-7	nitrobenzene	202-716-0	98-95-3	Carc. 2 Repr. 1B Acute Tox. 3 Acute Tox. 3 Acute Tox. 3 STOT RE1 Aquatic Chronic 3	H351 H360F H301 H311 H331 H372 (blood) H412	GHS06 GHS08 Dgr	H351 H360F H301 H311 H331 H372 (blood) H412			

The amended classification for nitrobenzene introduced with Reg (EC) 944/2013 (5th ATP to Regulation (EC) 1272/2008) applies from 1st of January 2015. An extract of the corresponding RAC opinion¹ is given in Annex I.

3. Environmental fate properties

Not relevant for the identification of the substance as SVHC in accordance with Article 57 points (a) to (c) REACH.

4. Human health hazard assessment

Not relevant for the identification of the substance as SVHC in accordance with Article 57 points (a) to (c) REACH.

5. Environmental hazard assessment

Not relevant for the identification of the substance as SVHC in accordance with Article 57 points (a) to (c) REACH.

¹ <http://echa.europa.eu/documents/10162/58b183f8-3178-4a37-a4fe-68385af2cbf8>

6. Conclusions on the SVHC Properties

6.1. CMR assessment

Nitrobenzene is covered by index number 609-003-00-7 of Regulation (EC) No 1272/2008 in Annex VI, part 3, Table 3.1 (the list of harmonised classification and labelling of hazardous substances) and it is classified in the hazard class reproductive toxicity category 1B (H360F 'May damage fertility').

Therefore, this classification of the substance in Regulation (EC) No 1272/2008 shows that it meets the criteria for classification in the hazard class:

- Reproductive toxicity category 1B in accordance with Article 57 (c) of REACH.

6.2. PBT and vPvB assessment

Not relevant

6.3. Equivalent level of concern assessment

Not relevant

Part II

7. Manufacture, import and export

Nitrobenzene has been registered as mono-constituent substance seven times for intermediate uses; one registration is for on-site isolated intermediates and six registrations are for use as transported isolated intermediates under strictly controlled conditions.

The companies as listed at the ECHA dissemination site are given below:

- A) AFKEM AG Erdmannstr. 10, 22765, Hamburg, Germany
- B) BASF Antwerpen N.V. Haven 725, Scheldelaan 600, 2040, Antwerpen 4 Antwerpen, Belgium
- C) Bayer Antwerpen NV Scheldelaan 420 Haven 507, 2040, Antwerpen, Belgium
- D) Bayer MaterialScience AG Kaiser-Wilhelm-Allee, 51368, Leverkusen, Germany
- E) BorsodChem MCHZ Chemická 1/2039, 709 03, Ostrava, Czech Republic
- F) DOW OLEFINVERBUND GMBH Strasse B 13, D-06258, Schkopau, Germany
- G) HUNTSMAN Polyurethanes (UK) Ltd Haverton Hill Road, TS23 1PS, Billingham, United Kingdom

The following company has registered nitrobenzene as full, individual submission. To a great extent the registration comprises intermediate uses under SCC:

- H) CUF-Quimicos Industriais, Quinta da Industria Beduido, 3860-680, Estarreja Portugal

8. Information on uses of the substance

8.1. Overview of uses

General description of manufacture and uses of Nitrobenzene

Nitrobenzene is manufactured by nitration of benzene with a mixture of concentrated sulfuric acid, water, and nitric acid. The reaction is considered to be dangerous due to the high exothermicity of the reaction ($\Delta H = -117$ kJ/mol).

Most nitrobenzene produced is converted to aniline, which has many downstream products. Aniline is manufactured by hydrogenation of nitrobenzene in the presence of metal catalysts (typically at 200–300 °C). Lower volumes, but nevertheless important, industrial outlets include electrolytic reduction to 4-aminophenol, nitration to give 1,3-dinitrobenzene, chlorination to give 3-chloronitrobenzene, sulfonation to give 3-nitrobenzenesulfonic acid, and chlorosulfonation to give 3-nitrobenzenesulfonyl chloride. The last three products are consumed mainly as their reduction products, 3-chloroaniline, metanilic acid, and 3-aminobenzenesulfonamide, respectively (Ullmann's, 2011).

Use information from registrant(s)

Nitrobenzene is mainly used for the production of other substances. The major part of the substance is thus used as an intermediate under strictly controlled conditions (SCC). The registration dossiers report both industrial and professional uses. No consumer uses are registered. Table 4 lists those registered uses.

Table 4: Uses

	Use(s)
Manufacture	Manufacturing of Nitrobenzene, intermediate for further chemical processing
Formulation	Industrial formulation using laboratory chemicals
Uses at industrial sites	Manufacturing of Nitrobenzene, intermediate for further chemical processing Industrial manufacture of laboratory chemicals and intermediates Industrial use of a laboratory chemical as a processing aid Industrial use in the manufacture of pharmaceuticals Industrial Manufacture – Intermediate Use Manufacture of Bulk Large Scale Chemicals – Intermediate Use Manufacture of Fine Chemicals – Intermediate Use
Uses by professional workers	Professional use of laboratory chemicals Professional use in the manufacture of pharmaceuticals
Consumer Uses	--
Article service life	---

Use information from SPIN database

The SPIN database² summarises information on substances in different products on the national markets of Norway, Sweden, Finland and Denmark.

According to the Danish database in 2013 nitrobenzene was present in 23 products in Denmark with an amount of smaller than 0.1 tons. In 2000 nitrobenzene was present in 31 products and a peak of nitrobenzene in products is noted in 2006, where nitrobenzene was present in 81 products on the market of Denmark. Due to information provided in the SPIN database nitrobenzene is present in reprographic agents in the printing industry (from 2000 to 2010). No further details are provided on use sectors of nitrobenzene in the year 2012.

In Norway, Sweden, Finland no nitrobenzene containing products were listed at this time.

Use information from Poland

According to the Polish register based on article 45 of CLP regulation there is 1 entity which produces 11 mixtures and imports 1 mixture containing nitrobenzene. Those mixtures were registered as intermediate/laboratory chemicals for industrial and professional uses. This information is available only for the year 2013. No information about tonnages is available.

² Substances in Preparations in the Nordic countries
<http://195.215.251.229/DotNetNuke/-default.aspx> (accessed 05.05.2015))

8.2. Substance use as intermediate

8.2.1. Description of use

Nitrobenzene is mainly used for the production of other substances. The major part of the substance is used as an intermediate under strictly controlled conditions (SCC). Intermediate uses under non-strictly controlled conditions are registered as well. These intermediate uses appear to be not within the scope of the authorisation requirement according to Article 8 (b) of the REACH Regulation.

8.2.2. Locations and quantities used

(Removed due to confidentiality)

8.2.3. Recent and future trends

No information is available. As the substance is a raw material for the manufacture of other high volume chemicals, manufacture and consumption are considered to be in the same order of magnitude like the current tonnages.

8.2.4. Structure of supply chain

No information is available.

8.3. Substance use as non-intermediate

8.3.1. Description of use

The non-intermediate uses cover: use for the preparation of formulations, use as processing aid and use as solvent.

8.3.2. Locations and quantities used

Only a low tonnage of the total tonnage is presently used as non-intermediate. *(Further details have been removed due to confidentiality).*

8.3.3. Recent and future trends

(Further details have been removed due to confidentiality).

8.3.4. Structure of supply chain

No information is available.

8.4. Imports and exports of articles into and from the EU

Most of the manufactured tonnage is used and consumed as intermediate for the production of other high production chemicals. No information is available for articles.

9. Release and exposure from uses

9.1. Human exposure from Industrial uses

Workplace monitoring

No monitoring data are available in the registrations. All exposure estimates are based on modelling. However, in the EU Risk Assessment Report (RAR, 2007) workplace monitoring data for the production of nitrobenzene and the further processing to aniline have been submitted (RAR, 2007). The exposure levels of nitrobenzene in 1990 to 1997 were up to 3.5 mg/m³ (177 samples), with the 90th percentile of 0.25 mg/m³.

Intermediate use under strictly controlled conditions

For intermediate use under strictly controlled conditions (SCC) a limited set of data is required according to REACH Article 17 (Registration of on-site isolated intermediates) and Article 18 (Registration of transported isolated intermediates).

Registration dossiers must contain details on risk management measures applied by the manufacturer and information on risk management measures recommended for the user (for transported isolated intermediates). If the registrant can demonstrate that SCC are applied, quantitative exposure assessment and risk characterisation are not required. Thus, for intermediate use under SCC, no quantitative exposure assessments are provided by the registrants, as exposure is considered to be negligible by them.

Full registration, individual submission

The following six exposure scenarios, for which no strictly controlled conditions are considered, have been described and assessments have been performed by the registrant:

- Industrial manufacture of laboratory chemicals and intermediates
- Industrial use of a laboratory chemical as a processing aid
- Industrial formulation using laboratory chemicals
- Industrial use in the manufacture of pharmaceuticals
- Professional use of laboratory chemicals
- Professional use in the manufacture of pharmaceuticals

9.2. Human exposure from Professional uses

Referring to the registration data, professional use was indicated for the use of the substance as laboratory chemical and manufacture of pharmaceuticals. Both uses target handling of the substance by non-industrial professionals in laboratories or in industrial settings.

9.3. Consumer uses

Consumer uses are not registered by the Registrant(s) and were not identified.

9.4. Releases from use of articles

No information is available.

9.5. Releases from the waste stage

No information is available.

9.6. Summary of releases

Industrial and professional uses were registered by the Registrant(s). Consumer uses were not registered and are not assessed by the Registrant(s).

The greatest part of the manufactured tonnage is used as intermediate use under strictly controlled conditions (SCC) according to REACH Article 17 and Article 18. Nevertheless, intermediate uses under non-strictly controlled conditions and non-intermediate uses are registered as well.

No monitoring data are available in the registrations. All exposure estimates are based on modelling. However, in the EU Risk Assessment Report (RAR, 2007) workplace monitoring data for the production of nitrobenzene and the further processing to aniline have been submitted (RAR, 2007). The exposure levels of nitrobenzene in 1990 to 1997 were up to 3.5 mg/m³ (177 samples), with the 90th percentile of 0.25 mg/m³.

10. Current knowledge on alternatives

10.1. Introduction

10.1.1. Intermediate use

Nitrobenzene is an important feedstock for the production of chemicals (most important aniline) and pharmaceuticals. For the production of aniline (a raw material for the manufacture of MDI, rubber processing chemicals, herbicides, dyes and pigments and speciality fibres) an alternative process avoiding nitrobenzene is available. There aniline (and the by-product diphenylamine) is formed by vapour-phase ammonolysis of phenol, using an alumina catalyst (Kent, 2010).

10.1.2. Non-intermediate use

The use as solvent has become less important in the past years. For the preparation of formulations, the uses as laboratory chemical, processing aid and in the manufacture of pharmaceutical substances no detailed information on technical processes is available. Therefore, evaluation of alternatives is difficult.

10.2. Literature review

To get further information on non-intermediate uses and possible replacements a rough internet investigation/literature search has been carried out and provided evidence that:

- According to literature (White, 2008) nitrobenzene is or has been used as

plasticizer for PVC. Dependent on the solvent quality needed other plasticizers (beside phthalates, e.g. butyl acetate) are available.

- Nitrobenzene is or has been used for the refining of lubricants (solvent extraction)³. Lubricant is mixed with nitrobenzene and after some time then the liquid separates into two layers: Solvent layer containing impurities and oil layer free from impurities. Other possible less toxic solvents are mixtures of propane and cresol or sulphur dioxide.
- Replacement in laboratory use is already ongoing in some fields (e.g. its use in lignin analysis (Masingale, 2009))

10.3. Information from consultation

(Further details have been removed due to confidentiality).

10.4. Conclusions on alternatives

No information on alternatives has been provided by the Registrant(s). Information was collected from literature or internet sources. The use as solvent has become less important in the past years. For the preparation of formulations, the uses as laboratory chemical, processing aid and in the manufacture of pharmaceutical substance no detailed information on technical processes is available. Therefore evaluation of alternatives is difficult.

11. Existing EU legislation

Nitrobenzene is covered by index number 609-003-00-7 in Annex VI, Table 3.1 of CLP Regulation (EC) No 1272/2008 amended by Regulation (EC) No 944/2013 (5th ATP)⁴.

An EU wide indicative occupational exposure limit (OEL) value (8h TWA 0.2ppm; skin notation) has been set by Commission Directive 2006/15/EC⁵ and other measures to protect workers from risks related to exposure to nitrobenzene are in place^{6,7}. The indicative OEL has been taken over by AT, BE, FIN, FR, DE, HU, IT, LV, PL, ES, NL and UK. However, DK and SE have set a higher limit value of 1 ppm (5 mg/m³). Additional short term exposure levels have been set by AT, DK, FIN, DE, and SE⁸.

In the frame of the Existing Substances Regulation (ESR) (EEC) No 793/93 a detailed risk assessment has been carried out (RAR, 2007) by the German CA.

Regulation (EC) 1223/2009 lists Nitrobenzene in Annex II, list of substances prohibited

³ <http://de.slideshare.net/jatingarg52/lubrication-45792262>;

<http://www.machinerylubrication.com/Read/28960/mineral-oil-refining>

⁴ Commission Regulation (EU) No 944/2013 of 2 October 2013 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures

⁵ Commission Directive 2006/15/EC of 7 February 2006 establishing the second list of indicative occupational limit values in implementation of Council Directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work.

⁶ Council Directive of June 1989 on the introduction of measures to encourage improvements in the safety and health of workers at work (89/391/EEC).

⁷ Council Directive 98/24/EC of April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/291/EEC).

⁸ Source: BIA GESTIS International limit values (accessed on 28th July 2015)
http://limitvalue.ifa.dguv.de/WebForm_ueliste2.aspx

in cosmetic products.

12. Previous assessments by other authorities

Hazard and risk assessments have been conducted previously to characterise the potential adverse effects of nitrobenzene to human health and/or environment and to give recommendations to limit the health risks due to nitrobenzene exposure (RAR, 2007; WHO, 2003).

12.1. Existing Substance Program (Reg (EEC) No 793/93)

Under the former Existing Substances Program a risk assessment report (RAR) was published (RAR, 2007). For the environment it was demonstrated that the PEC/PNEC ratios based on site specific assessments are below 1 suggesting a low risk for all compartments. Based on the risk evaluation it was concluded and agreed by the scientific committee on health and environmental risks (SCHER) that, for the environment part at the time of evaluation, there is no need for further information and/or testing and for risk reduction measures beyond those which are being applied already (RAR, 2007; EC, 2005).

Concerning human health, in the RAR a data gap for skin sensitisation was identified, due to absence of reliable studies. The identified data gap has been closed. In the frame of REACH registration a local lymphnode assay has been submitted, which demonstrates that nitrobenzene has no sensitising potential (Vohr, 2008).

The exposure assessment for workers in the RAR refers to production of nitrobenzene and further processing as a chemical intermediate in the large-scale chemical industry only.

The risk characterisation performed in the RAR for human health used the margin of safety (MOS) approach. It was concluded that for reproductive and developmental toxicity there has been at the time of evaluation no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already, since the MOS are large (Conclusion II). Concerning repeated dose toxicity and carcinogenicity the experts concluded, that there is need for limiting the risks, and risk reduction measures which are already being applied shall be taken into account, since the margin of safeties (MOS) are low (Conclusion iii).

It is concluded in the RAR that on the background of cancer risks, air concentrations of nitrobenzene at the workplace should be controlled to a level in the range of 0.1 mg/m³ (critical exposure level for carcinogenicity). Concerning local effects after repeated exposure the critical exposure level with a value of 0.07 mg/m³ is even lower. If the exposure is reduced to this level, inhalation risks from other endpoints, as systemic repeated dose toxicity would similarly and effectively be mitigated too. Also skin contact with nitrobenzene should be reduced. Based on the cancer risk assessment dermal exposure should be controlled to levels in the range of 0.03 mg/kg/day or 2.1 mg/person/day.

12.2. Harmonized classification based on Reg (EC) No 1272/2008

In the year 2012 Germany has submitted a CLH dossier for nitrobenzene (ECHA, 2012a). Nitrobenzene had already an Annex VI entry in the CLP Regulation, where it had been classified as Repr. 2 H361f beside other endpoints. RAC re-evaluated the hazard data for nitrobenzene on the basis of numerous developmental toxicity studies, which have been

conducted in the years 1983 to 1995.⁹ RAC concluded that there is sufficient evidence that nitrobenzene needs to be classified for Repr. 1B (H360 F). (please refer to Annex I)

12.3. WHO Environmental Health Criteria Programme

In 2003 a WHO report (Environmental Health Criteria 230) for nitrobenzene has been published (WHO, 2003). Experts evaluated the risks of nitrobenzene exposure for human health and environment. For the occupational setting the experts recommended that the exposures should be kept as low as possible using the best available technology, and a valid method of biological monitoring is recommended. The experts stated, that beside adequate safety training of workers, the monitoring of nitrobenzene-exposed workers and record-keeping of workplace exposure are needed. Furthermore it was suggested that epidemiological studies on working population should be conducted. It was also suggested that nitrobenzene should be removed from consumer products wherever possible and that contaminated areas (such as landfill sites) should be identified, and appropriate surveillance and introduction of measures to control emissions to air and water should be instituted.

13. Executive summary of information on manufacture, use, exposure and alternatives

13.1. Manufacture, imports and exports

High tonnages of the substance are manufactured in the EU. The substance is registered currently by eight Registrants. Only a low tonnage is imported into the EU. (*Further details have been removed due to confidentiality*).

13.2. Uses

Nitrobenzene is mainly used for the production of other substances. The major part of the substance is used as an intermediate under strictly controlled conditions (SCC). Intermediate uses under non-strictly controlled conditions are registered as well. Uses as non-intermediate are for the preparation of formulations, use as processing aid and use as solvent. Only industrial and professional uses are registered. Consumer uses are not registered and were not identified.

13.3. Releases from manufacture and use

The greatest part of the manufactured tonnage is used as intermediate under strictly controlled conditions (SCC) according to REACH Article 17 and Article 18. Nevertheless, intermediate uses under non-strictly controlled conditions and non-intermediate uses are registered as well.

No monitoring data for non-intermediate uses are available in the registrations. All exposure estimates are based on modelling. However, in the EU Risk Assessment Report (RAR, 2007) workplace monitoring data for the production of nitrobenzene and the further processing to aniline have been submitted (RAR, 2007). The exposure levels of nitrobenzene in 1990 to 1997 were up to 3.5 mg/m³ (177 samples), with the 90th percentile of 0.25 mg/m³.

⁹ Studies were conducted prior to the ESR RAR (RAR, 2007) and to the SCOEL (SCOEL, 2002) evaluation

The CSR reports risk characterization ratios close to but lower than 1 for intermediate and non-intermediate uses. These results must be taken with caution because of lacking detailed descriptions and of shortcomings. There is a potential for concern, when taking into account the low DNEL values derived and the exposure levels provided in RAR, 2007. *Additional information has been removed due to confidentiality.*

13.4. Current knowledge of alternatives

Evaluation of alternatives is difficult as for the relevant non-intermediate uses no information on technical processes is available. Only limited information is available in open sources but indications for possible replacement could be found. No information from Registrant(s) is available.

REFERENCES

References for Part I

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References for Part II

EC (European Commission) (2005). Scientific committee on health and environmental risks (SCHER). Opinion on "Risk assessment report on Nitrobenzene: Environmental Part". CAS: 98-95-3, EINECS No.: 202-716-0, pp. 5.

ECHA (2012a). Nitrobenzene. Committee for Risk Assessment. Annex 1. Background document to the opinion proposing harmonised classification and labelling at Community level (ECHA/RAC/CLH-O-0000002350-87-01/A1)

ECHA (2012b). Nitrobenzene. Committee for Risk Assessment. Opinion proposing harmonised classification and labelling at Community level. (ECHA/RAC/CLH-O-0000002350-87-01/F)

Kent J.A. (2010). Kent and Riegel's Handbook of Industrial Chemistry and Biotechnology. Springer Science & Business Media. ISBN: 978-0-387-27842-1

Masingale M.P., Alves E.F., Korbieh T.N., Bose S.K., Francis R.C. (2009). An oxidant to replace nitrobenzene in lignin analysis. *BioResources* 4(3), 1139-1146.

RAR – European Union Risk Assessment Report (2007). Nitrobenzene, CAS No: 98-95-3, EINECS No: 202-716-0. Volume 77; 3rd priority list

SCOEL (2002). Recommendation from the Scientific Committee on Occupational Exposure Limits for nitrobenzene. SCOEL/SUM/93/July 2002. pp.9

Ullmann's Encyclopedia of Industrial Chemistry, 7th Edition (2011), ISBN: 978-3-527-32943-4

Vohr HW (2008). Nitrobenzene: Local lymph node assay in mice (LLNA/IMDS). Testing laboratory: Bayer HealthCare AG, Special Toxicology, Wuppertal, Germany. Report no.: AT04707. Owner company: ISOPA, Brussels, Belgium, as cited in the REACH registration dossier.

White J.L., Kim K-J (2008). Thermoplastic and rubber Compounds: Technology and physical Chemistry. Carl Hanser Verlag, Munich.

WHO (2003). Environmental Health Criteria 230. Nitrobenzene. Office of chemical Safety Therapeutic Goods Administration, Australian Department of Health and Ageing, Canberra, Australia. pp. 265

Please note – Annexes containing confidential information have been removed.

Annex I - Additional information on Nitrobenzene

Extract of the RAC opinion¹⁰ on C&L of Nitrobenzene

(ECHA/RAC/CLH-0-0000002350-87-01/F)

Evidence has been provided (...) that the reduced male fertility and/or atrophy of spermatogenic epithelium, or degeneration of tubular epithelium in testes were observed at exposure levels inducing low increase of methemoglobin concentration in blood (...). The damage to spermatogenic epithelium and reduced fertility is a specific effect of nitrobenzene independent from its ability to induce MetHb and related hematotoxic effects. RAC is of the opinion that there is sufficient evidence to classify nitrobenzene according to the CLP regulation for the reproductive toxicity category 1B (Presumed human reproductive toxicant) with hazard statement H360F (Repr. 1B, H360F) and according to Directive 67/548 to Repr. Cat. 2, R60 –May impair fertility.

RAC is of the opinion that nitrobenzene should not be classified within CLP or DSD system for lactation effects as alterations in viability and body weight gain of pups observed in rats during lactation were due to severe maternal toxicity (ECHA, 2012b).

¹⁰ <http://echa.europa.eu/documents/10162/58b183f8-3178-4a37-a4fe-68385af2cbf8>

Annex IV - Data on uses

Overview of Uses¹¹

For nitrobenzene, a full registration and registrations for intermediate use were submitted. Referring to both types of registrations, the substance is mainly used for the industrial production of other substances under SCC. Referring to the full registration, uses under non-strictly controlled conditions exist. These uses are synthesis (intermediate) uses under non-SCC, use for the preparation of formulations, use as processing aid and use as solvent. The uses and corresponding process categories of the registrations are summarised in Table 5 and Table 6 below.

Table 5: Use(s) and corresponding categories from intermediate registrations

	Use(s)
Manufacture	<p>Manufacturing of Nitrobenzene, intermediate for further chemical processing</p> <p>PROC 1: Use in closed process, no likelihood of exposure PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation)</p> <p>ERC 1: Manufacture of substances ERC 6a: Industrial use resulting in manufacture of another substance (use of intermediates)</p>
Uses at Industrial Sites	<p>Manufacturing of Nitrobenzene, intermediate for further chemical processing</p> <p>PROC 1: Use in closed process, no likelihood of exposure PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities PC 19: Intermediate ERC 1: Manufacture of substances ERC 6a: Industrial use resulting in manufacture of another substance (use of intermediates)</p>
Consumer Uses	Not registered.
Article service life	Not registered.

ERC: environmental release category, PC: product category, PROC: process category

¹¹ The dissemination site was accessed on 19th of May 2015.

Table 6: Use(s) and corresponding categories from full registration

	Use(s)
Manufacture	<p>Industrial manufacture of laboratory chemicals and intermediates</p> <p>PROC 1: Use in closed process, no likelihood of exposure PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) PROC 4: Use in batch and other process (synthesis) where opportunity for exposure arises PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing) PROC 15: Use as laboratory reagent</p> <p>ERC 1: Manufacture of substances</p> <p>ERC 6a: Industrial use resulting in manufacture of another substance (use of intermediates)</p> <p>ERC 6b: Industrial use of reactive processing aids</p> <p>Industrial use in the manufacture of pharmaceuticals</p> <p>PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) PROC 4: Use in batch and other process (synthesis) where opportunity for exposure arises PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing) ERC 1: Manufacture of substances ERC 4: Industrial use of processing aids in processes and products, not becoming part of articles ERC 6a: Industrial use resulting in manufacture of another substance (use of intermediates) ERC 7: Industrial use of substances in closed systems</p> <p>Industrial Manufacture – Intermediate Use</p> <p>PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) ERC 1: Manufacture of substances ERC 4: Industrial use of processing aids in processes and products, not becoming part of articles</p> <p>Manufacture of Bulk Large Scale Chemicals – Intermediate Use</p> <p>PROC 1: Use in closed process, no likelihood of exposure</p>

	Use(s)
	<p>ERC 1: Manufacture of substances ERC 4: Industrial use of processing aids in processes and products, not becoming part of articles</p> <p>Manufacture of Fine Chemicals – Intermediate Use</p> <p>PROC 1: Use in closed process, no likelihood of exposure PROC 3: Use in closed batch process (synthesis or formulation) ERC 1: Manufacture of substances ERC 4: Industrial use of processing aids in processes and products, not becoming part of articles ERC 6a: Industrial use resulting in manufacture of another substance (use of intermediates) ERC 7: Industrial use of substances in closed systems</p>
Formulation	<p>Industrial formulation using laboratory chemicals</p> <p>PROC 1: Use in closed process, no likelihood of exposure PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) PROC 4: Use in batch and other process (synthesis) where opportunity for exposure arises PROC 5: Mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact) PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing) PROC 15: Use as laboratory reagent PC 21: Laboratory chemicals ERC 2: Formulation of preparations</p>
Uses at industrial site	<p>Industrial manufacture of laboratory chemicals and intermediates</p> <p>PROC 1: Use in closed process, no likelihood of exposure PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) PROC 4: Use in batch and other process (synthesis) where opportunity for exposure arises</p> <p>PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing) PROC 15: Use as laboratory reagent</p> <p>PC 19: Intermediate</p>

Use(s)
<p>PC 21: Laboratory chemicals</p> <p>ERC 1: Manufacture of substances ERC 6a: Industrial use resulting in manufacture of another substance (use of intermediates) ERC 6b: Industrial use of reactive processing aids</p> <p>Industrial use of a laboratory chemical as a processing aid</p> <p>PROC 15: Use as laboratory reagent PC 21: Laboratory chemicals ERC 4: Industrial use of processing aids in processes and products, not becoming part of articles</p> <p>Industrial use in the manufacture of pharmaceuticals</p> <p>PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) PROC 4: Use in batch and other process (synthesis) where opportunity for exposure arises PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing) PC 29: Pharmaceuticals ERC 1: Manufacture of substances ERC 4: Industrial use of processing aids in processes and products, not becoming part of articles ERC 6a: Industrial use resulting in manufacture of another substance (use of intermediates) ERC 7: Industrial use of substances in closed systems</p> <p>Industrial manufacture – Intermediate Use</p> <p>PROC 2: Use in closed, continuous process with occasional controlled exposure</p> <p>PROC 3: Use in closed batch process (synthesis or formulation) PC 19: Intermediate ERC 1: Manufacture of substances ERC 4: Industrial use of processing aids in processes and products, not becoming part of articles</p> <p>Manufacture of Bulk Large Scale Chemicals – Intermediate Use</p> <p>PROC 1: Use in closed process, no likelihood of exposure PC 19: Intermediate ERC 1: Manufacture of substances</p> <p>ERC 4: Industrial use of processing aids in processes and products, not becoming part of articles</p>

	Use(s)
	<p>Manufacture of Fine Chemicals – Intermediate Use</p> <p>PROC 1: Use in closed process, no likelihood of exposure PROC 3: Use in closed batch process (synthesis or formulation) PC 19: Intermediate ERC 1: Manufacture of substances ERC 4: Industrial use of processing aids in processes and products, not becoming part of articles ERC 6a: Industrial use resulting in manufacture of another substance (use of intermediates) ERC 7: Industrial use of substances in closed systems</p>
Uses by professional workers	<p>Professional use of laboratory chemicals</p> <p>PROC 1: Use in closed process, no likelihood of exposure PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) PROC 4: Use in batch and other process (synthesis) where opportunity for exposure arises PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities PROC 10: Roller application or brushing PROC 15: Use as laboratory reagent</p> <p>PC 21: Laboratory chemicals</p> <p>ERC 9a: Wide dispersive indoor use of substances in closed systems ERC 8a: Wide dispersive indoor use of processing aids in open systems ERC 8b: Wide dispersive indoor use of reactive substances in open systems</p> <p>Professional use in the manufacture of pharmaceuticals</p> <p>PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities PC 29: Pharmaceuticals ERC 1: Manufacture of substances ERC 4: Industrial use of processing aids in processes and products, not becoming part of articles ERC 6a: Industrial use resulting in manufacture of another substance (use of intermediates) ERC 7: Industrial use of substances in closed systems</p>
Consumer Uses	Not registered.

Article service life	Use(s)
	Not registered.

ERC: environmental release category, PC: product category, PROC: process category