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Joint Research Centre

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European Chemicals Bureau
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BUT-2-YNE-1,4-DIOL

CAS No: 110-65-6

EINECS No: 203-788-6

Summary Risk Assessment Report

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SUMMARY RISK ASSESSMENT REPORT

Final report, 2005

Germany

Rapporteur for the risk assessment of but-2-yne-1,4-diol is the Federal Institute for Occupational Safety and Health.

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PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance but-2yne-1,4-diol that has been prepared by Germany in the context of Council Regulation (EEC) No. 793/93 on the evaluation and control of existing substances.

For detailed information on the risk assessment principles and procedures followed, the underlying data and the literature references the reader is referred to the comprehensive Final Risk Assessment Report (Final RAR) that can be obtained from the European Chemicals Bureau[1]. The Final RAR should be used for citation purposes rather than this present Summary Report.

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

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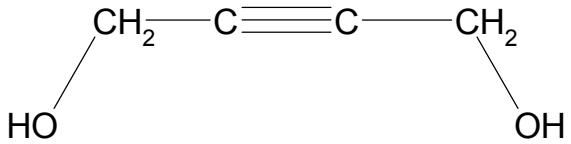
TABLES

1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS Number: 110-65-6
EINECS Number: 203-788-6
IUPAC Name: But-2-yne-1,4-diol
Synonyms: 1,4–Butynediol, 1,4–Dihydroxy–2–butyne, 2–Butyne–1,4–diol, 2–Butynediol, Bis(hydroxymethyl)acetylene, But–2–in–1,4–diol, Butindiol, Butynediol
Molecular weight: 86.09 g/mol
Empirical formula: $C_4H_6O_2$
Structural formula:



1.2 PURITY/IMPURITIES, ADDITIVES

Purity: 98.5-99.5%
Impurities: < 0.5% water
1% butane-1,4-diol
Additives: no additives

1.3 PHYSICO-CHEMICAL PROPERTIES

Table 1.1 Physico-chemical properties

Property	Value
Physical state	at 20°C and 1,013 hPa: yellow scaly solid
Melting point	58°C
Boiling point	> 200°C (238°C) decomposition relatively slowly between 160 and 200°C, violent above 200°C
Relative density	1.114 at 20°C
Vapour pressure	0.17 Pa at 20°C
Surface tension	58.9 mN/m at 30.8°C (50% aqueous solution)
Partition coefficient	logPow -0.73 at 25°C (OECD 107)
Water solubility	ca. 750 g/l solution at 20°C 20 g/l solvent at 0°C 3,740 g/l solvent at 25°C
Flash point	not determined (solid)
Auto flammability	no self ignition up to the decomposition

Table 1.1 continued overleaf

Table 1.1 continued Physico-chemical properties

Property	Value
Flammability	not highly flammable (Annex V, 67/548/EEC)
Explosive properties	not explosive
Oxidising properties	no oxidising properties

Boiling point

The boiling point submitted by one producer (GAF-Huels, 1994) was given as 238°C. In the literature a decomposition of the substance is noted above 160°C. The decomposition process starts relatively slowly between 160 and 200°C, and becomes violent above 200°C.

Vapour pressure

The vapour pressure was estimated according to Clausius-Clapeyron using values between 88.3 and 238 degrees (GAF-Huels (1994), Beilstein (1974), Kirk-Othmer (1991)) without regarding the crystallisation of butynediol. The problem in such cases is the uncertainty of an estimation of values over a very large temperature range.

Water solubility

The solubility is given as value of 750 g/l solution at 20°C, which was used for the calculations. The value of 3,740 g/l solvent at 25°C converted into g/solution is comparable to the first mentioned value.

1.4 CLASSIFICATION

Classification according to Annex I of Directive 67/548/EEC

Classification

T; R 23/25 Toxic by inhalation and if swallowed

C; R 34 Causes burns

Xn: R 48/22 Harmful: danger of serious damage to health by prolonged exposure if swallowed

Xn; R 21 Harmful in contact with skin

Xi; R 43 May cause sensitisation by skin contact

Specific Concentration limits

C ≥ 50%: T, C; R 21-23/25-34-48/22-43
25% ≤ C < 50%: T; R 21-23/25-36/38-48/22-43
10% ≤ C < 25%: Xn; R 20/22-48/22-43
3% ≤ C < 10%: Xn; R 20/22-43
1% ≤ C < 3%: Xi; R 43

Labelling

C; T

R: 21-23/25-34-43-48/22

S: (1/2)-25-26-36/37/39-45-46

According to the data presented below and the criteria of Directive 67/548/EEC, butynediol has not to be classified as dangerous to the environment.

2 GENERAL INFORMATION ON EXPOSURE

At two sites in the European Union butynediol is produced at tonnages of > 1,000 tonnes/annum, the maximum production volume at a single site is 100,000 tonnes/annum.

The maximum cumulative production volume as indicated in IUCLID amounts to 200,000 tonnes/annum, from 1993 to 1996 around 185,000 tonnes were annually produced. Less than 300 tonnes/annum were exported outside the European Union.

Butynediol is produced by Reppe synthesis from acetylene and formaldehyde.

The main application area (> 98%) of butynediol is hydrogenation to butanediol and butenediol; both substances are used as chemical intermediates.

Less than 2% (< 3,700 tonnes/annum) of the butynediol produced are not used as internal intermediate but sold to external processing sites for the production of flame retardants or as a corrosion inhibitor and pickling agent in metal surface treatment.

Besides this, butynediol is reported to serve as an intermediate for the synthesis of polyols, insecticides, pharmaceuticals and auxiliaries for the paint and textile industry.

From the information available in the product registers butynediol is understood to be a component in cleaning solutions to remove scale by means of acids, in acid pickles and in organic paint removers. A total amount of 10 tonnes/annum were identified to be contained in products on the Danish, Swedish and Norwegian market. The following consumer products may contain butynediol:

- Cleansing agents for sanitary installations (conc. < 2%)
- Car cleansing products (conc. < 1%)
- Building facade cleansers (conc. < 3%)
- Disinfectants for sanitary installations (0.33-2%)
- Pipe descaling agents (0.15-1%)
- Descaling agents (0.2-1%)

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

Releases of butynediol into the environment are expected from production and processing with wastewater and, to less extent, exhaust gases.

Further releases are expected through the use in metal surface treatment and of cleaning agents.

Releases to the soil compartment via sludge application may only occur from municipal sewage treatment plants (STP), because at both production sites the sewage sludge is incinerated.

Residual butynediol-contents in the final products can not be quantified but are expected to be not significant. Butanediol contain generally less than 0.0001% of butynediol and the residual content in butenediol is less than 0.05%.

The environmental behaviour of butynediol is determined by the following characteristics:

- the estimated atmospheric half-life is approximately 11 hours,
- butynediol is readily biodegradable, no data are available on hydrolysis,
- evaporation from surface water is not an important fate process,
- the estimated K_p values indicate no relevant adsorption onto sediment or soil.

Based on the physical chemical properties of butynediol, the hydrosphere is the preferred target compartment and neither relevant bioaccumulation nor geoaccumulation is expected. In wastewater treatment plants (STPs) 87.3% of the substance are estimated to be removed by biodegradation, 12.7% are released to surface water.

Predicted Environmental Concentrations (PECs) are calculated for the local aquatic environments of the production and processing sites using both, default release estimates and site specific effluent measurements because the latter only were of spot check character. The resulting concentrations in surface water are 6.5 µg/l and 196 µg/l for the default estimates and 0.32 µg/l and 0.22 µg/l based on the spot check measurement.

As butynediol is also used as an external intermediate, a default calculation for external processing is performed leading to a local concentration of 2.1 µg/l.

For the use of butynediol in metal surface treatment releases are expected that lead to local surface water concentrations of 6.3 µg/l.

For the use of consumer products that may contain small quantities of butynediol a quantitative local exposure assessment seems not necessary.

No monitoring data in the aquatic environment are available.

For the sediment compartment no PEC-estimation is performed, because relevant adsorption of butynediol onto sediment is not expected.

For the atmosphere a generic PEC estimation representing a realistic worst case for external processing is performed because releases from both production sites are significantly lower (< 25 kg/annum each according to their official emission declaration for the local authorities). A maximum concentration in air in the vicinity of that site of 0.03 µg/m^3 is estimated.

Exposure of the soil may only occur through atmospheric deposition after local release to the atmosphere. No direct releases had been identified and the input through sludge application on agricultural soil is considered negligible.

From the total annual deposition in the vicinity of the generic external processing site the maximum equilibrium concentration in soil is calculated. The resulting bulk concentration in soil (natural soil and agricultural soil) amounts to 0.015 µg/kg the respective porewater concentration is 0.1 µg/l.

The regional background concentrations are calculated according to EUSES:

$$PECregional_{aquatic} = 0.28\ \mu g/l$$
$$PECregional_{air} = 2.6 \cdot 10^{-9}\ \mu g/m^3$$
$$PECregional_{soil} = 1.8 \cdot 10^{-4}\ \mu g/kg\ ww$$

3.2 EFFECTS ASSESSMENT

Only results from acute toxicity tests with species from 3 trophic levels are available.

For fish one test was conducted on *Pimephales promelas* (96-hour LC50 = 53.6 mg/l) and two tests had been performed on *Leuciscus idus* (48-hour LC50 = 82 mg/l and 46.4 mg/l < 96-hour LC50 < 100 mg/l).

The most sensitive organism from standard tests is the invertebrate *Daphnia magna* (48-hour EC50 = 26.8 mg/l).

Aquatic plants showed significantly less sensitivity. For *Scenedesmus subspicatus* a 72-hour EC50 value of 483.7 mg/l and a 96-hour EC50 value of 433.1 mg/l are recorded for cell growth.

In non-standard tests the lowest acute toxicity is recorded for *Xenopus laevis* (96-hour LC50 = 15.5 mg/l, larval toxicity).

For the calculation of the Predicted No Effect Concentration (PNEC) the lowest LC50 of 15.5 mg/l obtained with *Xenopus laevis* is used although the test was not conducted with adult animals, because the value is sufficiently supported by the effect concentration observed with *Daphnia magna*.

As there are no long-term test results available, the assessment factor is set at AF = 1,000. The fact that test with *Xenopus* was not conducted with adult animals is no justification to decrease the assessment factor.

Therefore a $PNEC_{aqua}$ of 15.5 mg/l / 1,000 = 15.5 µg/l is derived.

For microorganisms in a test with *Pseudomonas putida* according to Bringmann-Kuehn after 17 hours an EC50 of 3,935 mg/l and an EC10 of 1993 were obtained for cell multiplication inhibition. In addition, a population growth impairment test was done in a *Tetrahymena pyriformis* batch system. An IG50 of 1,343 mg/l after 48 hours was obtained.

For assessing the toxicity of a substance to microorganisms to identify adverse effects in STPs, an assessment factor in the range of 1 to 100 is applied for tests on microorganisms with different sensitivity and different endpoints.

On the EC10-value for *Pseudomonas putida* an assessment factor of 1 can be applied resulting in a PNEC $_{microorganisms}$ of 1,993 mg/l.

But also *Tetrahymena pyriformis,* a protozoa found in STPs, is relevant for the assessment, although this species does not influence the degradation processes itself, but nevertheless is needed for the proper function of a STP. With the appropriate assessment factor of 10 to be applied on the EC50 of 1,343 mg/l a $PNEC_{microorganisms}$ of 134 mg/l is obtained.

There are no experimental results with benthic organisms available and there is no need for performing an indicative quantitative risk assessment for the sediment compartment, because butynediol shows no relevant adsorption onto sediment.

It is not possible to derive a PNEC for the atmospheric compartment due to the lack of experimental data.

Valid experimental data on effects of butynediol in terrestrial organisms are not available. For an indicative risk assessment for the soil compartment, the aquatic PNEC can be used and compared to the concentration in soil pore water: $PNEC_{soil,\ porewater}$ = 15.5 µg/l.

In addition, there are indications that butynediol inhibits the nitrification of NH_4-N in soil. From the results with two different types of soil it is possible to deduce an EC50-value between 50 and 100 mg/kg. An assessment factor of 1,000 is applied to determine the $PNEC_{soil}$ for the inhibition of nitrification: $PNEC_{soil}$ = 50 µg/kg dw.

As butynediol does not present indications of a bioaccumulation potential, an effect assessment for secondary poisoning is not required.

3.3 RISK CHARACTERISATION

3.3.1 Aquatic compartment (incl. sediment)

The possible risks to microorganisms in wastewater treatment plants are evaluated for municipal and industrial facilities. For all considered scenarios the PEC/PNEC ratios are far below one and a risk for the function of the STPs is not expected. **Conclusion (ii)**.

For surface water a comparison between PEC and PNEC for all relevant exposure scenarios is performed. Only for one production site a risk for the local aquatic environment is identified on the basis of default release estimates (PEC/PNEC = 13). However, recently performed effluent measurements indicate actual releases far below the default assumptions leading to a PEC/PNEC ratio of 0.03. Although the measurements are of spot check character it can be anticipated that an unacceptable risk for the aquatic environment is unlikely. There is therefore no need for further testing and/or gathering of exposure information. **Conclusion (ii)**.

From the current manufacturing and use of butynediol no risk for the sediment compartment is expected. **Conclusion (ii)**.

3.3.2 Atmosphere

Due to the short atmospheric lifetime ($t_{1/2}$ = 11 hours) and low emissions to air, adverse effects on organisms and abiotic effects upon the atmosphere, like global warming and ozone depletion are not expected from butynediol. **Conclusion (ii)**.

The vapour pressure of butynediol is 0.17 Pa at 20C and therefore significantly below the trigger value for substances to be regarded a *volatile organic compound* (VOC). The contribution to photochemical smog production can be assumed to be very low. **Conclusion (ii)**.

3.3.3 Terrestrial compartment

The risk characterisation is performed for the generic exposure scenario representing a worst case situation in the vicinity of an external processing site.

From an indicative risk assessment (equilibrium partitioning method) no risk is deduced for the soil (porewater) compartment on the basis of the aquatic PNEC (PEC/PNEC = 0.007, **Conclusion (ii**)) and the same result is obtained if the assessment is based on the inhibition of nitrification for bulk soil (PEC/PNEC = 0.0004, **Conclusion (ii)**).

3.3.4 Secondary poisoning

As butynediol does not present indications of a bioaccumulation potential, a risk characterisation for secondary poisoning is not required. **Conclusion (ii)**.

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

4.1.1.1 Occupational exposure

Butynediol is mainly used as an internal chemical intermediate to produce butanediol and butenediol (approximately 98%). The remainder (approximately 2%) is used as flakes and aqueous solutions (32-34%) in further processing to polyols, auxiliaries for the paint industry and flameproofing agents as well as in the production of formulations. The most frequent product types are metal surface treatment and acidic cleaning solutions in which butynediol is used as an additive.

Detailed information on the production volumes is given in Section 2.

Based on the available information the following scenarios are regarded to be relevant for occupational exposure:

- Production of butynediol and further processing as an intermediate (Scenario 1, 2)
- Preparation of formulations, e.g. pickling, descaling solutions (Scenario 3, 4)
- Use of acid pickling and Ni-plating baths in the electroplating industry (Scenario 5 – 8)
- Use in organic paint removers (Scenario 9)
- Use in acidic solutions for the removal of scale (Scenario 10, 12)
- Use in acidic solutions for the removal of rust (Scenario 11, 13)

Further applications of butynediol are possible, e. g. in car cleaning agents and sanitary disinfectants. Since these use patterns are very seldom, the corresponding exposure situations are judged to be of minor relevance for butynediol.

Occupational exposure limit values (OEL) are not known.

The exposure assessment is based on measured data and literature data, expert judgement and estimations according to the EASE model (Estimation and Assessment of Substance Exposure). The exposure levels should be regarded as reasonable worst-case estimates representing the highly exposed workers.

The results for the different scenarios are summarised in **Table 4.1**.

Inhalation exposure

With regard to possible exposure to butynediol, three exposure situations are observed:

- use of formulations / solutions without the formation of droplet aerosols
- use of solutions / formulations with the formation of aerosols
- use of butynediol as flakes with the formation of dusts

Most scenarios cover the handling of formulations without the formation of droplet aerosols (Scenario 1-4, 6 and 8-13). These scenarios include the production of butynediol solutions, the use of solutions for acidic pickling and nickel plating, the use of organic paint removers and acidic solutions for the removal of rust and scale. In all cases, based on the low vapour pressure of the substance (0.17 Pa) inhalation exposure is assessed to be very low. In addition

to exposure to vapour, for the use of butynediol solutions/formulations in acidic pickling processes and during nickel plating (Scenario 5, 7) the formation of droplet aerosols is regarded to be a probable situation and inhalation exposure to aerosols is assessed as well. The basis for this assessment is surrogate data and expert judgement.

Beside the production of butynediol solutions butynediol is also produced as flakes (Scenario 2). The corresponding exposure assessment for inhalation to dust is made based on measurement data. The flakes are used to produce formulations (Scenario 3). For this scenario, exposure is assessed based on the EASE model.

Dermal exposure

With regard to dermal exposure, measured results are not available. For most occupational exposure scenarios, the regular use of suitable PPE (Personal Protective Equipment) at the workplaces is not probable. Therefore, actual dermal exposure is generally assessed based on the EASE model without considering that PPE might be worn by a part of the exposed collective. In general, dermal exposure is assessed as exposure to part of hands and forearms.

Within the framework of the assessment of dermal exposure, the corrosivity of pure butynediol and of formulations containing more than 50% of the substance is taken as an indication of low dermal exposure and a low contact level is chosen (EASE model: incidental; Scenario 1-3). This procedure is also applied in case of formulations like e.g. acidic cleaning solutions which are assumed to act as corrosive because of corrosive properties of other ingredients (Scenario 5, 6, 9). For all other scenarios (4, 7, 8, 10, 11, 12, 13), dermal exposure is assessed for the unprotected worker.

Summary of exposure data

The results are summarised in **Table 4.1**. The main sources of inhalation exposure are drumming (Scenario 2) and of dermal exposure filling works (Scenario 4).

Table 4.1 Summary of exposure data

Exposure scenario	Duration and frequency of activities relevant for exposure	Inhalation exposure Shift average [mg/m³]	Dermal exposure Shift average [mg/person/day]
Production and further processing / Further processing to formulations			
1) Large-scale chemical industry (solution, 34% butynediol)	shift length, daily	very low [1)]	0-13 [2)]
2) Large-scale chemical industry (e.g. flakes)	shift length (exp. judg.), daily	1 [3)]	0-42 [2)]
3) Preparation of formulations (e.g. flakes)	1 hour/day, 30 days/year	a) 0.14(with LEV) [4)] b) 0.6without LEV) [4)]	0-42 [2)]
4) Preparation of formulations (solution, 34% butynediol)	1 hour/day, 30 days/year	very low [1)]	14.3-143 [4)] (irregular use)
Use of formulations			
5) Acid pickling processes (0.5% butynediol)	shift length (assumed), daily	0.12 [3)]	0-0.21 [5)]

Table 4.1 continued overleaf

Table 4.1 continued Summary of exposure data

Exposure scenario	Duration and frequency of activities relevant for exposure	Inhalation exposure Shift average [mg/m3]	Dermal exposure Shift average [mg/person/day]
Use of formulations			
6) Acid pickling processes (0.5% butynediol)	shift length (assumed), daily	very low [1)]	0-0.21 [5)]
7) Nickel plating (0.03% butynediol)	shift length (assumed), daily	0.002 [3)]	0.1-0.13 [4)]
8) Nickel plating (0.03% butynediol)	shift length (assumed), daily	very low [1)]	0.025-0.25 [4)]
9) Organic paint removers (10% butynediol)	shorter than shift length (assumed), daily	very low [1)]	0-4.2 [5)]
10) Acidic solutions for the removal scale (0.2% butynediol; industrial sector)	shift length (assumed), occasionally	very low [1)]	0.08-0.84 [4)]
11) Acidic solutions for the removal of rust (0.2% butynediol; industrial sector)	shift length (assumed), daily	very low [1)]	0.08-0.84 [4)]
12) Acidic solutions for the removal scale (0.2% butynediol; skilled trade sector)	shift length (assumed), occasionally	very low [1)]	0.84-4.2 [4)]
13) Acidic solutions for the removal of rust (0.2% butynediol; skilled trade sector)	shift length (assumed), daily	very low [1)]	0.84-4.2 [4)]

LEV local exhaust ventilation
PPE personal protective equipment (here gloves)
1) Expert judgement (low vapour pressure of the pure substance of 0.17 Pa), rough estimation: < 0.04 mg/m³
2) Dermal exposure for incidental contacts with corrosive substance / formulations
3) Exposure assessment based on expert judgement, analogy consideration
4) Exposure assessment based on model estimates (EASE model)
5) Expert judgement (with respect to the corrosive properties of other substances in the solution)

4.1.1.2 Consumer exposure

Butynediol serves as a component of consumer products for the following uses: cleansing agents and disinfectants for sanitary installations (conc. < 2%), car cleansing products (conc. < 1%), and descaling agents for tiles (conc. < 1%).

Inhalation exposure

- Cleansing agents and disinfectants for sanitary installations

For estimation of inhalation exposure to butynediol of this use the application of an amount of 100 g of cleansing agent/disinfectant containing 2% butynediol (dilution factor 100) onto an area of 2 m² is considered. Assuming a daily use with a duration time of 10 minutes and a contact time of 2 hours for this scenario a mean event concentration of 0.00014 mg/m³ and a cumulative (worst-case) dose of 0.007 µg/kg bw/day were calculated.

- Car cleansing products

Assuming the weekly use of an amount of 100 g of cleansing agent containing 1% of butynediol inside a car with a duration time of 10 minutes results in a cumulative worst-case estimate of 0.004 µg/kg bw/day, whereas an average concentration of $2.6 \cdot 10^{-3}$ mg/m³ was calculated for inhalation exposure.

- Descaling agents

For this scenario the application of an amount of 100 g of a descaler containing 1% of butynediol onto an area of 2 m² is considered. Assuming usage twice per month for 10 minutes with a contact time of 2 hours a cumulative worst-case dose estimate of 0.02 µg/kg bw/day is calculated due to exposure via inhalation with an average event concentration of 0.007 mg/m³.

Total inhalation exposure of the consumer

The cumulative inhalation exposure of the consumer to butynediol calculated for all kinds of use is estimated to be in range of about 0.03 µg/kg bw/day (yearly average). For risk assessment purposes the inhalation exposure by use of descaling agents with a mean concentration 0.00014 mg/m³ has been taken into account.

Dermal exposure

- Cleansing agent and disinfectants for sanitary installations

The use of the Consexpo program reveals a dermal exposure of 0.0003 mg/kg bw/day. The absorption fraction is approximated to 1% in relation to the contact time of 10 minutes assuming 100% absorption within 24 hours. The calculation is based on the assumption that no protective clothing e.g. gloves are used. It can be assumed that the exposure may be much lower if protecting cloth is worn.

- Car cleansing products

For this use a dermal exposure of 0.00024 mg/kg bw/day is calculated. The absorption fraction is estimated to about 1% for a contact time of 10 minutes assuming 100% absorption within 24 hours. The calculation is based on the assumption that no protective clothing e.g. gloves are used. Otherwise, the exposure may be much lower.

- Descaling agents

For this use a dermal exposure of 0.0001 mg/kg/day is calculated. The absorption rate (related to a duration of 10 minutes) has been estimated to about 1%, which is based on an assumed absorption of 100% within 24 hours. The calculation is again based on the assumption that no protective clothing e.g. gloves are used. Otherwise, the exposure may be much lower.

Total dermal exposure of the consumer

The resulting total dermal exposure of the consumer to butynediol containing products will be in a range of about 0.0006 mg/kg bw/day.

Total exposure of the consumer

For risk characterisation related to chronic exposure, a value of ~ 0.67 µg/kg bw/day is carried forward which is calculated as a daily dose from inhalation and dermal exposure.

4.1.1.3 Humans exposed via the environment

Indirect exposure to humans via the environment is calculated using data for intake via drinking water, food and air.

The main route of indirect exposure is the intake via stem for the local scenario (0.004 mg/kg bw/day). The regional scenario leads to a predominant intake via drinking water (0.008 µg/kg bw/day).

4.1.2 Effects assessment

Absorption of butynediol via the oral and dermal routes is demonstrated in animals, absorption via the lungs has been shown recently in an acute inhalation toxicity study. Specific investigations about toxicokinetic behaviour and metabolism are not available. It can be anticipated, that in a first metabolic step butynediol is enzymatically activated in liver by alcoholdehydrogenase to the corresponding reactive aldehyde capable of reacting with biologically relevant nucleophiles. Cytochrome P450-dependent metabolism can not be excluded.

Human data on acute toxicity caused by butynediol are not available. Butynediol is toxic after oral administration (oral LD50, rat: 132 to 176 mg/kg bw) and by inhalation (LC50, rat: 0.69 mg/l/4hours), and harmful following dermal absorption of aqueous solutions (dermal LD50, rat: 659 to 1,240 mg/kg bw). Liver and kidneys were the primary targets and different stages of degeneration, including necrosis, were observed. Based on the acute toxicity data for inhalation and oral administration, classification as toxic and labelling with R 23/25 (“toxic by inhalation and if swallowed”) is warranted. According to the data for dermal exposure butynediol is labelled with R 21 (“harmful in contact with skin”).

Human data on local irritancy/corrosivity are not available. Pure undiluted butynediol has proven to cause corrosion by contact with skin. No irritant effects on rabbit skin were observed with 20% and 40% butynediol solutions. In contact with eyes the substance can cause irreversible corneal opacity. Therefore, butynediol is classified as corrosive (C) and causes burns (R 34).

In man, two cases of contact allergy caused by butynediol have been described. Animal data on three Magnusson Kligman tests demonstrate that the substance shows a weak sensitisation potential. Based on the human experience showing the occurrence of contact allergy at the workplace the substance has been classified as “sensitising” and labelled with R 43 – “May cause sensitisation by skin contact”. There is no information available on respiratory sensitisation.

There is no information on the health effects in humans of repeated exposure to butynediol.

An oral 28-day study on rats revealed toxic effects on liver, kidney, and hematopoietic system at doses from 10 mg butynediol/kg bw/day. The dose of 50 mg/kg bw/day caused mortality in males and females. Histopathology showed congested internal organs, pulmonary oedema and severe changes in liver and kidneys, which included diffuse hepatic parenchymal necrosis, accompanied by reactive mononuclear cells and granulocytes, fatty changes, as well as renal tubular degeneration and interstitial mononuclear cell infiltration in the kidney. An oral NOAEL of 1 mg/kg bw/day was derived from the oral 28-day study. A preliminary concern on neurotoxicity from an oral 6-month study with reduced reliability was not confirmed by the results from a 30-day inhalation study on rats that included a battery of examinations on the neurofunction and motor activity and histopathology of the nervous system.

Indications of local toxic effects on the respiratory tract were observed on 30-day liquid aerosol exposure to rats: Epithelial changes of the nasal cavity at 100 mg/m³ and above, tracheal inflammation at 25 mg/m³, and metaplasia and inflammation of the larynx at 5 mg/m³ and above. The NOAEC for systemic toxicity was 25 mg/m³; the NOAEC for local effects on the respiratory tract was 0.5 mg/m³. Inhalation exposure on 5 days to butynediol aerosol resulted also in inflammation and metaplasia of the laryngeal mucosa at concentrations of 25 mg/m³ and above. The liver and kidney were also affected by repeated inhalation exposure on 5 days at a concentration of 300 mg/m³. Additionally this concentration caused some treatment-related deaths, growth retardation and, in unscheduled deaths only, toxic effects on the spleen, thymus and gastrointestinal tract.

Butynediol showed no genotoxic potential in a bacterial gene mutation test. An equivocal result was obtained with regard to induction of chromosomal aberrations *in vitro*. *In vivo*, a bone marrow micronucleus test was negative for doses up to the toxic range. Altogether, there is no relevant concern with respect to germ cell mutagenicity of butynediol.

There are no experimental data on the carcinogenic properties of butynediol available.

There are no human data available on toxicity for reproduction. Assessment of the available animal data from studies with rats does not indicate a specific toxic potential of butynediol adverse to reproduction and/or development including any teratogenic effects by the oral route of administration. Moreover, there are no indications for substance-related interference with spermatology and/or estrous cyclicity. Other routes of application have not been investigated. An oral NOAEL/fertility of 40 mg/kg bw/day was derived from a one-generation study (OECD Guideline 415) and an oral NOAEL/developmental toxicity of 80 mg/kg bw/day was derived from a developmental study according to OECD Guideline 414.

4.1.3 Risk characterisation

4.1.3.1 Workers

Butynediol is a solid substance with a vapour pressure of < 1 Pa at 20°C. Approximately 98% of butynediol is used as a chemical intermediate in manufacturing companies. About 2% of butynediol are sold in the form of flakes and as an aqueous solution for the production of further chemicals. Exposure routes to be considered at the workplace are inhalation (dust, aerosols and vapour) and skin contact to the solid substance (flakes) and to butynediol solutions. The toxicological profile of butynediol is essentially determined by its local toxicity (skin sensitisation, respiratory tract irritation, skin and eye irritation/corrosivity).

For toxicological endpoints with relevant quantitative data MOS values are calculated as quotient of experimental NOAEL (or LOAEL) and workplace exposure assessments. Scientifically based assessment factors describe the stepwise extrapolation of animal data to the worker population. The value of the minimal MOS, as decision mark between **conclusion (ii)** and **(iii)**, results from the multiplicative combination of the different assessment factors and the uncertainty factor. Minimal MOS values may be different for each toxicological endpoint. In a parallel procedure, which gives identical but more direct results, a "critical exposure level" is identified for each endpoint, indicating concern if occupational exposure levels exceed this value.

Butynediol risk assessment is based on the assumption of 100% absorption for all three routes of application (oral, inhalation, dermal). For extrapolation of oral or dermal data, metabolic

rate scaling results in 4-times lower effective dose levels in humans (in mg/kg/day) compared to rats. An additional uncertainty factor is determined which takes into account several aspects, as for instance the reliability of the data base, the biological relevance of the observed effects, the slope of the dose response curve or the variability of the human population.

The following risks at the workplace are considered specifically for each toxicological endpoint. A summary table containing all scenarios at risk is given at the end of this section.

Acute toxicity

Conclusion (ii)

Acute systemic effects were not detected at the experimental exposure level of 100 mg/m³ (results from a 5-day dose finding study). For Scenario 2, the workplace scenario with the highest exposure level by inhalation (1 mg/m^3) the MOS value of 100 is calculated.

The highest dermal exposure level of 14.3-143 mg/person/day is calculated for the preparation of formulations (34% solution). The lowest MOS, based on the upper range of the EASE estimate, calculates to 323. Based on the proposal of a minimal MOS of 100 there seems to be no concern for acute dermal toxicity for all exposure scenarios.

No additional concern for combined exposure is indicated.

Irritation/corrosivity

Acute Respiratory Tract Irritation

Conclusion (iii)

The subacute NOAEC for local effects in the respiratory tract is 0.5 mg/m³, the corresponding LOAEL with marginal to slight effects is 5 mg/m³. For acute inhalation, the level of 5 mg/m^3 might be very near to the NAEC for local effects. A minimal MOS of 4 is proposed for acute irritation by inhalation (a factor of 2 to reflect 8-hour exposure and light activity of workers multiplicated with a factor of 2 revealing remaining uncertainties that the starting point of 5 mg/m^3 is a clear NAEC). The corresponding critical exposure level is about 1 mg/m³.

The highest exposure level of 1 mg/m³ results in the lowest MOS of 5; for this borderline situation concern is indicated.

Dermal and eye irritation

Conclusion (ii)

Butynediol itself is a corrosive substance. Concentrations of greater than 50% are considered to be corrosive, concentrations between 25% and 50% are assumed to be irritative to skin and eye. In some areas of production and use handling of corrosive material is assumed. If the required protection (based on current R34 classification) is strictly adhered to, **conclusion (ii)** for corrosivity is justifiable.

A solution with 34% of butynediol is considered to be irritating to skin and eyes. Non-proper handling of this solution (Scenario 1 and 4) cannot be excluded. If the required protection (based on current R36/38 classification) is strictly adhered to, **conclusion (ii)** for skin and eye irritation is justifiable.

Sensitisation

Skin sensitisation

Conclusion (iii)

It can be concluded from results of three Magnusson Kligman tests that butynediol possesses a weak skin sensitisation potential. Based on the human experience showing some cases of contact allergy at the workplace butynediol has been classified and labelled as a skin sensitiser; the general concentration limit of 1% for skin sensitisation was considered adequate for butynediol. Against that background of information concern is derived for all dermal exposure scenarios with a butynediol concentration greater than 1%.

Respiratory Sensitisation

Conclusion (ii)

There are no animal data available on respiratory sensitisation. For preliminary risk assessment butynediol is not suspected to be a respiratory sensitiser, thus corresponding risk due to inhalation exposure is not considered to be of concern.

Repeated Dose Toxicity

Local effects by repeated inhalation

Conclusion (iii)

The NOAEC for local effects on the respiratory tract taken forward to risk assessment is 0.5 mg/m^3 (subacute rat inhalation study).

Factors to be taken into account during MOS evaluation are: A factor of 2 is used for adjustment for breathing volumes. A factor of 1 is chosen for duration adjustment. There is a dose difference of one order of magnitude between the NOAEC and LOAEC; furthermore, there are only minimal to slight local effects at the LOAEC of 5 mg/m³ and at 25 mg/m³. Thus the actual NAEC might be higher than the experimental NOAEC. This aspect is taken into account with an adjustment factor of ½. Additionally there is an overall uncertainty factor of 3.

Thus, the minimal MOS calculates to 3 (2 · ½ · 3). Based on the starting point of 0.5 mg/m³ as NOAEC used for the calculation of MOS values, the corresponding 'critical exposure level' at the workplace is about 0.2 mg/m³. The exposure Scenario 2 "large-scale chemical industry dust resulting from handling of butynediol flakes" and Scenario 3b "preparation of formulations (dust) without LEV" are considered to be of concern.

Systemic effects by repeated inhalation exposure

Conclusion (ii)

Based on the subacute inhalation study in rats the NOAEC of 25 mg/m^3 is used for calculation of MOS values for systemic effects. For evaluation of MOS values adjustment factors may be taken into account: A factor of 2 accounts for adjustment of breathing volumes. The factor for duration adjustment is proposed to be 2. It is proposed to use an overall uncertainty factor of 3. Multiplication of these factors results in an overall factor of 12 which is identical to the minimal MOS of 12. The "critical exposure level" that triggers concern is about 2 mg/m^3. Based on the minimal MOS of 12 there is no exposure scenario that leads to concern.

Systemic effects by repeated dermal contact

Conclusion (ii)

Because of lack of relevant dermal toxicity data dermal risk assessment is based upon the subacute inhalation data. Thus, the starting point for calculation of MOS values is based upon the subacute NOAEC of 25 mg/m^3 (6 hours/day).

25 mg/m^3 corresponds to an intake by inhalation of 7.2 mg/kg/day (respiratory rate of 0.8 l/min/kg for the rat, 6 hours/day). Assuming a human body weight of 70 kg, a NAEL of 504 mg/p/d is calculated as starting point for dermal risk assessment.

For the evaluation of MOS values, the following factors are proposed: A factor of 4 is used for metabolic rate scaling. For duration adjustment a factor of 2 is taken. The default uncertainty factor is 5. An overall assessment factor of 40, which is identical to the minimal MOS, is calculated. The most critical dermal exposure scenario with a daily frequency of exposure of 13 mg/person/day is Scenario 1 (production of the 34% solution of butynediol in the large-scale chemical industry). This exposure level is considered to be a borderline situation. Because there is some evidence that bioavailability following dermal contact might be lower than by inhalative or oral exposure, it is proposed not to derive concern for this and all other dermal exposure scenarios with daily frequency of exposure.

Local effects by repeated dermal contact

Conclusion (ii)

For butynediol specific experimental data on local effects by repeated dermal contact are not available. If the required protection (based on current R36/38 classification) is strictly adhered to, **conclusion (ii)** for skin and eye irritation by repeated dermal contact seems to be justifiable.

Repeated dose toxicity: Combined exposure

Conclusion (ii)

No specific concern is derived for scenarios for combined exposure.

Mutagenicity and Carcinogenicity

Conclusion (ii)

In vitro, butynediol showed no genotoxic potential in a bacterial gene mutation test. Likewise induction of chromosomal aberrations was found to be negative. Also the *in vivo* bone marrow micronucleus test was negative.

Data concerning carcinogenicity are not available. Based on results of mutagenicity testing butynediol is not anticipated to be a genotoxic carcinogen. No concern is derived for mutagenicity or carcinogenicity.

Fertility Impairment and Developmental toxicity

Conclusion (ii)

For both types of reproductive toxicity studies with rats showed the identical NOAEL of 40 mg/kg/day. This NOAEL is higher than the NOAEL of 7.2 mg/kg/day, which was taken as

basis for the calculation of MOS values for repeated dose toxicity. It has to be stressed that a specific reprotoxic potential of butynediol has not been identified.

Summary

For butynediol an overall **conclusion (ii)** is reached for all toxicological endpoints except for a) local effects in the respiratory tract by acute and repeated inhalation exposure and b) skin sensitisation. Butynediol is a corrosive material and is considered to be irritating to the eye and skin in a concentration range of 25 to 50%. It is assumed that control measures exist which, if implemented and complied with, reduce the risk of skin and eye irritation/corrosivity.

Conclusions for all occupational exposure scenarios are listed in **Table 4.2**

Table 4.2 Conclusions for all occupational exposure scenarios

Exposure Scenarios			Local effects by acute inhalation	Local effects by repeated inhalation	Sensiti-sation	Other toxico-logical endpoints
Production and further processing						
1	Large-scale chemical industry (vapour/ 34% solution)				iii	
2	Large-scale chemical industry, flakes, with LEV		iii	iii	iii	
Further processing to formulations						
3 a/b	Preparation of formulations (dust)	a) + LEV			iii	
		b) - LEV		iii		
4	Preparation of formulations (vapour/ 34% solution)				iii	
Use of formulation						
5	Acid pickling processes (content: 0.5%, corrosive because other ingredients) (aerosol)		conclusion (ii) for all other scenarios	conclusion (ii) for all other scenarios		conclusion (ii) for all other scenarios
6	Acid pickling processes (vapour/ 0.5% solution, corrosive because other ingredients)					
7	Ni-plating (content: 0.03%) (aerosol)					
8	Ni-plating (vapour/ 0.03%solution)					
9	Organic paint removers (vapour/ 10% solution) corrosive because other ingredients				iii	
10	Acidic solutions for the removal of scale (industrial area) (vapour/ 0.2% solution)				conclusion (ii) for all other scenarios	
11	Acidic solutions for the removal of rust (industrial area) (vapour/ 0.2% solution)					
12	Acidic solutions for the removal of scale (skilled trade) (vapour/ 0.2% solution)					
13	Acidic solutions for the removal of rust (skilled trade) (vapour/ 0.2% solution)					

Regarding respiratory tract irritation, risk reduction measures are considered to be necessary for those exposure scenarios in which butynediol is handled as solid substance (Scenario 2 and 3b). Concern is expressed for repeated inhalation exposure (both scenarios) and for acute

inhalation exposure (Scenario 2). The other exposure scenarios with handling of liquid butynediol preparations are not judged to be of concern. Based on available toxicity data, local effects in the respiratory tract are considered to be more critical than the corresponding systemic effects. This difference in potency is visualised by the critical exposure levels of 0.2 mg/m^3 for local effects by repeated exposure and of 2 mg/m^3 for systemic effects.

In addition to its substantial irritation potential (skin, eye, respiratory tract) butynediol has been proved to be a weak skin sensitiser. Concern has been derived for the exposure scenarios with butynediol itself and preparations with a butynediol concentration greater than 1%.

4.1.3.2 Consumers

Consumer exposure to butynediol may occur via inhalation and dermally as a result of use of cleansing agents and disinfectants for sanitary installations, car cleansing products, and descaling agents for tiles. For the combined exposure to the substance in these products an exposure in the range of about 1 µg/kg bw/day is estimated. During application of cleansing agents the consumer may be exposed to a concentration of 0.014 mg/m^3 butynediol for a contact time of 10 minutes.

Repeated dose toxicity

- Total exposure via inhalation and dermal route

Proper use of the cleansing agents/disinfectants products, car cleansing products, and descaling agents will result in a cumulative butynediol exposure (worst-case) in the range of about 0.67 µg/kg bw/day.

In repeated dose toxicity studies on rats (30-day inhalation) the NOAEC for systemic effects was 25 mg/m³ which can be converted to a NOAEL of 7.2 mg/kg bw/day estimating the inhaled amount of the substance using the respiratory minute volume 0.8 l/min/kg and exposure duration of 360 minutes/day. The margin of safety between the exposure estimate and the NOAEL is judged to be sufficient taking in account all assumptions being applied in the exposure estimations. **Conclusion (ii)**.

- Local respiratory effects due to inhalation

During application of descaling agents the consumer may be exposed to a concentration of 0.007 mg/m^3 butynediol for a contact time of 10 minutes. Increasing concentrations of butynediol induced local toxic effects on the respiratory tract consisting of metaplasia and inflammation in the larynx, trachea, and nasal cavity on 30-day inhalation exposure of rats. The NOAEC for effects on the larynx was 0.5 mg/m^3. The adverse effects in the larynx were graded minimal to slight at the LOAEC of a 5 mg/m³. The margin of safety between the calculated exposure and the NOAEC for local effects by repeated exposure is judged to be sufficient taking into account all assumptions being applied in the exposure estimation scenario as well as the lacking steep dose response-relationship for local respiratory effects. **Conclusion (ii).**

Reproductive Toxicity

From the results of a one-generation drinking water study on rats (OECD Guideline 415) an oral NOAEL/fertility of 40 mg/kg bw/day was derived. An oral NOAEL/developmental toxicity of 80 mg/kg bw/day was obtained from a gavage teratology study on rats according to OECD Guideline 414. Taking into account the estimated low exposure in the range of about 1 µg/kg bw/day it can be concluded that the margins of safety for reproductive effects are

considered to be sufficient. Thus, there is no concern in relation to consumer exposure. **Conclusion (ii)**.

4.1.3.3 Humans exposed via the environment

Indirect exposure via the environment is calculated using data for intake via drinking water, food and air. An intake of a total daily dose of 0.004 mg/kg bw/day is calculated for the local scenario and of 0.008 µg/kg bw/day for the regional scenario.

Repeated dose toxicity

For the risk characterisation the total daily intake for the local and the regional scenario is compared with an oral NOAEL of 1 mg/kg bw/day which was derived from an oral 28-day rat study. The margins of safety expressed by the magnitude between the calculated exposure values and the NOAEL are considered to be sufficient for both scenarios. Thus, the substance is of no concern in relation to indirect exposure via the environment. **Conclusion (ii)**.

Reproductive Toxicity

From the results of a one-generation drinking water study on rats (OECD Guideline 415) an oral NOAEL/fertility of 40 mg/kg bw/day was derived. An oral NOAEL/developmental toxicity of 80 mg/kg bw/day was derived from a gavage teratology study on rats according to OECD Guideline 414. Taking into account the exposure values it can be concluded that the margins of safety for both the local and the regional scenario are considered to be sufficient. Thus, there is no concern in relation to indirect exposure via the environment. **Conclusion (ii)**.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

With regard to the physico-chemical properties and with regard to the occupational and consumer exposure described butynediol is not excepted to cause specific concern relevant to human health. **Conclusion (ii)**.

5 RESULTS

5.1 ENVIRONMENT

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 all environmental compartments.

5.2 HUMAN HEALTH

5.2.1 Human health (toxicity)

5.2.1.1 Workers

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

Regarding respiratory tract irritation, risk reduction measures are considered to be necessary for those exposure scenarios in which butynediol is handled as a solid substance (Scenario 2: production and further processing; Scenario 3b: preparation of formulations, without LEV). Concern is expressed for repeated inhalation exposure (both scenarios) and for acute inhalation exposure (only Scenario 2).

In addition to its substantial irritation potential (skin, eye, respiratory tract) butynediol has been proved to be a weak skin sensitiser. Concern has been derived for the exposure scenarios with butynediol itself and preparations with a butynediol concentration of greater than 1%.

For butynediol, occupational exposure limits are not reported. Within the context of Council Regulation 793/93 toxicological data have been generated that do allow the establishment of a health-based occupational exposure level.

5.2.1.2 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.

5.2.1.3 Humans exposed via the environment

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.

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.