FOREWORD INTRODUCTION

2-METHYL-3-YN-2-OL

CAS N°: 115-19-5

COVER PAGE

SIDS Initial Assessment Report
for
8th SIAM

(Paris, 28th – 30th October 1998)

Chemical Name: 2-Methylbut-3-yn-ol

CAS No.: 115-19-5

Sponsor Country: Germany

National SIDS Contact Point in Sponsor Country:

Mr. Jan Ahlers

HISTORY:

SIDS Dossier and Testing Plan were reviewed at the SIDS Review Meeting in September 1993 where the following SIDS Testing Plan was agreed:

no testing ( )
testing (X)

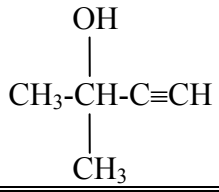
Tests on gene mutation in vivo and teratogenicity have been conducted

COMMENTS:

Deadline for circulation: 31st of July 1998

Date of circulation: 20th of July 1998
(To all National SIDS Contact Points and the OECD Secretariat)

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	115-19-5
Chemical Name	2-Methylbut-3-yn-2-ol
Structural formula	

CONCLUSIONS AND RECOMMENDATIONS

Environment: The chemical does reveal low ecotoxicity.PEC/PNEC ratios are less than 1. Therefore, it is currently considered of low potential risk and low priority for further work.

Health: The chemical is harmful after acute oral exposure and of low toxicity after dermal and inhalative exposure. In some cases skin and eye irritation were reported in workers. The chemical is a mild irritant after prolonged skin exposure. However, exposure for workers, consumers and populations via the environment is low in the Sponsor country. Therefore, it is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The production volume of 2-Methylbut-3-yn-2-ol in Germany was 1,000 - 5,000 t/a in 1991 In Germany, 80% (of maximum 5,000 t/a) of the 2-methylbut-3-yn-2-ol is used in chemical industry as an intermediate for scents, cosmetics, vitamins and plant-protective agents. The remaining 20% were used as stabilizer for 1,1,1-trichloroethane in a concentration range of 3-7% (v/v). 1,1,1-trichloroethane was industrially used for cleaning and degreasing of metal surfaces, electronic structural parts, polymers and films. As 1,1,1-trichloroethane is no longer used, the corresponding use of 2-methylbut-3-yn-2-ol has also been stopped.

In Switzerland, 5,000-10,000 t were produced in 1991 by one manufacturer as an intermediate only.

2-Methylbut-3-yn-2-ol is not readily biodegradable but is inherently removable from water. Based on its physico-chemical properties the hydrosphere is the preferred compartment. Local PECs were calculated for production and processing. The highest PEC_{local} of 34 µg/l was calculated for the Swiss production site using default parameters.

Short-term tests with fish, daphnids and algae are available. The most sensitive species was the marine invertebrate *Chaetogammarus marinus*. With an assessment factor of 1000 a $PNEC_{aqua}$ of 359 µg/l was derived.

Taking into account the systemic toxicity of 2-Methylbut-3-yn-2-ol, there is no reason for concern; the substance is of low potential risk and low priority for further work. The most sensitive NOAEL is derived from a 4 week oral gavage study in rats with a NOAEL of 50 mg/kg b.w. Taking an EHE of 1.35 mg/kg/d for workers into account, there is a MOS of 37. Via the environment a daily uptake of 0.001 mg/kg b.w. was calculated giving a MOS of 50,000.

IF FURTHER WORK IS RECOMMENDED, SUMMARISE ITS NATURE

2-Methylbut-3-yn-2-ol

CAS-NO.:115-19-5			PROTOCOL	RESULTS
PHYSICAL CHEMICAL				
2.1	Melting Point		NA	ca. 3 °C
2.2	Boiling Point		DIN 51 751	102-105 °C (at1013 hPa)
2.3	Density		DIN 51757	0.86 kg/m^3
2.4	Vapour Pressure		NA	2000 Pa at20 °C
2.5	Partition Coefficient (Log Pow)		OECD 107	0.318
2.6 A	Water solubility		NA	miscible at 20°C
ENVIRONMENTAL FATE / BIODEGRADATION				
3.1.1	Photodegradation		calc. (Atkinson)	In air $T_{1/2}$ = 2.2days
3.3	Transport and Distribution		calculated (fugacity level 1 type)	in air: 5.5 % In water 94.47 % in soil 0.02 % in sediment 0.01 %
3.5	Biodegradation		OECD 301 D	inherently degradable
ECOTOXICOLOGY (lowest effect concentrations only)				
4.1	acute/prolonged toxicity to fish	Pimephales promelas	ASTM recommendation	LC_{50} (96 hr) = 3290 mg/l
4.2	acute/prolonged toxicity to aquatic invertebrates (daphnia)	Chaetogammarus marinus	NA	EC_{50} (96 hr) = 359 mg/l
4.3	toxicity to aquatic plants e. g. algae	*Scenedesmus subspicatus*	UBA	IC_{50}(72 hr) > 500 mg/l
4.4	toxicity to microorganisms	*Pseudomonas putida*	DIN 38412	EC_{50} (17 hr) = 8600 mg/l

CAS-NO.:115-19-5		SPECIES	PROTOCOL	RESULTS
TOXICOLOGY				
5.1.1	acute oral toxicity	rat	NA	LD_{50} = 1420 mg/kg
5.1.2	acute inhalation toxicity	rat	OECD 403	LC_{50} > 21300 mg/m^3 (vapor)
5.1.3	acute dermal toxicity	rat	OECD 402	LD_{50} >2000 mg/kg
5.4	repeated dose toxicity	rat	NA	NOAEL =50 mg/kg
5.5	genetic toxicity in vitro			
	bacterial test (gen mutation)	Ames	NA	- (with metabolic activation) - (without metabolic activation)
	non-bacterial in vitro test (chromosomal abberations)			no data available
5.6	genetic toxicity in vivo	MNT mouse	OECD 474	-
5.8	toxicity to reproduction	/	/	NOEL = mg/kg (general toxicity) NOEL = mg/Kg (rep. tox. Parental) NOEL = mg/Kg (rep. tox. F1)
5.9	developmental toxicity / teratogenicity	rat	OECD 414/	NOAEL =130 mg/kg (maternal toxicity) NOAEL =130 mg/Kg (embryo-/fetotoxicity) no teratogenic effect
5.11	experience with human exposure			

SIDS Initial Assessment Report

1. Identity

Name:	2-Methylbut-3-yn-2-ol
Cas-No.:	115-19-5
Empirical formula:	C_5H_8O
Structural formula:	$HC\equiv C\text{-}C(CH_3)_2(OH)$
Synonyms:	Dimethylethynylcarbinol 1,1-Dimethyl-2-propyn-1-ol α, α-Dimethylpropargyl alcohol Dimethyleacetylenecarbinol Dimethylethynylmethanol
Degree of purity:	98.5% (w/w)

2. General Information on Exposure

In Germany, 2-methylbut-3-yn-2-ol is produced only by one manufacturer, the production level was 1,000-5,000 t in 1991. There is no information about export or import volumes available.

In Germany, 80% (of maximum 5,000 t/a) of the 2-methylbut-3-yn-2-ol is used in chemical industry as an intermediate for scents, cosmetics, vitamins and plant-protective agents. The remaining 20% were used as stabilizer for 1,1,1-trichloroethane in a concentration range of 3-7% (v/v). 1,1,1-trichloroethane was industrially used for cleaning and degreasing of metal surfaces, electronic structural parts, polymers and films. As 1,1,1-trichloroethane is no longer used, the corresponding use of 2-methylbut-3-yn-2-ol has also been stopped.

In Switzerland, 5,000-10,000 t were produced in 1991 by one manufacturer as an intermediate only. 100-500 t are produced in the USA, the use is unknown.

According to the National Agency of Environmental Protection in Denmark, products with a typical concentration of 25% 2-methylbut-3-yn-2-ol have been registered. Further information is not available.

During production in Germany, 590 kg/a are emitted into the air at production and processing. The substance is daily measured in the waste water treatment plant effluent: < 3.2 t/a were emitted into the receiving water in 1996.

By the Swiss manufacturer, 120 kg/a are emitted into the air and < 10 kg/a into the water during processing (no further data available).

3. Environment

3.1 Environmental Exposure

3.1.1 General Discussion

2-Methylbut-3-yn-2-ol is miscible with water at 20°C. Its vapour pressure is 20 hPa at 20°C. Based on the molecular structure, a Henry constant of 0.1 $Pa \cdot m^3 \cdot mol^{-1}$ is calculated according the model of Hine & Mookerjee. This value indicates that only a slow volatilization from water solution can be expected.

The log Pow is 0.318 (flask shaking method). This value indicates that there is no significant potential for bio- or geoaccumulation. There are no measured values for bio- or geoaccumula-tion available.

Based on the physico-chemical properties, the hydrosphere is the preferred compartment of 2-methylbut-3-yn-2-ol (Mackay I: 94.5%).

2-Methylbut-3-yn-2-ol is not readily biodegradable. A test on ready biodegradability showed a BOD/ThOD ratio of < 1% [1]. In a Zahn-Wellens test, 2-methylbut-3-yn-2-ol was eliminated up to 96% in 11 days [2]. The substance can therefore be considered as inherently removable from water. According to the model SIMPLETREAT, in wwpt's a removal rate of 41% is predicted.

The calculated half-life due to photochemical-oxidative degradation in the atmosphere by OH-radicals, according to the estimation method by Atkinson, is about 2.2 days.

3.1.2 Predicted Environmental Concentration

a) point emissions into hydrosphere

By the German manufacturer, during production and processing < 3.2 t/a are emitted into the receiving water which has a low flow (10%-ile) of 734 m^3/s. The predicted environmental concentration is

$$\mathbf{PEC} = \frac{3.2 \cdot 10^6 \text{ g/a}}{2.3 \cdot 10^{13} \text{ l/a}} = \mathbf{0.14 \ \mu g/l}$$

The emissions by the Swiss producer can only be estimated using default parameters. According to the EU Technical Guidance Documents [3] an emission rate during production of 0.3% of the production volume is assumed. Based on a maximum production volume of 10,000 t/a, 30 t/a are emitted into the waste water. Passing a treatment plant, 41% are eliminated, so 17.7 t/a are emitted into river Rhône. At its low flow (20 m^3/s in winter) (according to [4]), the PEC is

$$\mathbf{PEC} = \frac{17.7 \cdot 10^6 \text{ g/a}}{5.2 \cdot 10^{11} \text{ l/a}} = \mathbf{34 \ \mu g/l}$$

Considering the broad use pattern, it is assumed that only a small part of the 4,000 t/a is processed by the producers. We would consider the following worst case scenario according to the EU Technical Guidance Documents:

10% of the 4,000 t/a are processed by one manufacturer. With an emission rate of 0.7%, 2,8 t/a are emitted into the waste water. Assuming an elimination factor of 41%, processing during 300 d/a and a river flow of 60 m^3/s, the PEC is

$$\mathbf{PEC} = \frac{2.8\ t/a \cdot 0.59}{1.6 \cdot 10^{12}\ l/a} = \mathbf{1 \mu g/l}$$

b) point emission into atmosphere

By the German manufacturer, 590 kg/a are emitted into the air during production and processing. According to the model described in the EU Technical Guidance Documents, a PEClocal_air of 0.45 µg/m^3 is calculated.

3.2 Effects on the Environment

3.2.1 Aquatic Effects

Available data

The following ecotoxic effect concentrations for aquatic organisms are available:

a) toxicity to fish

Pimephales promelas	LC_{50} = 3,290 mg/l (96h)	[5]
Leuciscus idus	LC_{50} = 2,200-4,600 mg/l (96h)	[6]

b) toxicity to invertebrates

Daphnia magna	EC_{50} > 500 mg/l (24 and 48h)	[7]
"	EC_0 = 1,000 mg/l (48h)	[8]
"	EC_{100} = 3,200 mg/l (48h)	
(effect: immobilisation, several tests)		
Mysidopsis bahia	LC_0 = 100 mg/l (96h)	[8]
"	LC_{50} = 436 mg/l (96h)	
(marine organism)		
Chaetogammarus marinus	LC_0 = 100 mg/l (96h)	[8]
"	LC_{50} = 359 mg/l (96h)	
(marine organism)		

c) toxicity to algae

Scenedesmus subspicatus	EC_{50} > 500 mg/l (72h)	[9]
"	EC_{20} = 404 mg/l (72h)	
(effect: growth inhibition)		

d) toxicity to bacteria

Pseudomonas putida	EC_{50} = 8600 mg/l (17h)	[10]
"	EC_{10} = 6400 mg/l (17h)	
(effect: growth inhibition)		
Activated sludge	EC_{20} > 1,000 mg/l (30 min)	[11]

e) other organisms

Xenopus laevis (embryos)	LC_{50} = 9,205 mg/l (96h)	[12]
"	EC_{50} = 3,136 mg/l (96h)	
(effect: malformation)		

Determination of $PNEC_{aqua}$

According to the EU Technical Guidance Document, the value of the assessment factor F is to be determined to 1000 for the aquatic compartment, as only short-term toxicity tests of 3 trophic levels are available. The PNEC is calculated from the lowest effect concentration (*Chaetogammarus marinus*, 96h-LC_{50} = 359 mg/l) as follows:

PNEC = 359 mg/l / 1000 = **359 µg/l**

3.2.2 Terrestrial Organisms

There are no data available on terrestrial organisms.

3.3 Initial Assessment for the Environment

The PEC/PNEC ratios are calculated as follows:

	PEC [µg/l]	PEC/PNEC
German producer	0.14	$3.9 \cdot 10^{-4}$
Swiss producer	34	$95 \cdot 10^{-3}$
processing	1	$2.7 \cdot 10^{-3}$

As in all cases PEC << PNEC, a risk to the aquatic compartment is not to be expected. The calculated ratios are based on test results with marine organisms. Considering test results on freshwater organisms, the values would be even lower.

4. Human Health

4.1. Human Exposure

4.1.0 General Discussion

2-Methylbut-3-yn-2-ol is used as an intermediate for pharmaceuticals, flavor and fragrances, cosmetics, pesticides and dyestuffs. Its content in the endproducts is below 0.1% [29, 30].

4.1.1 Occupational Exposure

Between 1979 and 1997 a total of 50 analysis were performed at the workplace [30]. The average concentration in the air was 0.49 ml/m^3 equivalent to 9.42 mg/m^3 of 2-Methylbut-3-yn-2-ol. No MAK value has been established so far.

4.1.2 Consumer Exposure

For 2-Methylbut-3-yn-2-ol used as an intermediate a consumer use is not known. Based on the low content of 2-Methylbut-3-yn-2-ol in the final products (< 0.1%), a consumer exposure is negligible in this case.

4.1.3 Indirect Exposure via the Environment

The concentration in drinking water has been calculated according to the Technical Guidance Documents (TGD 1996). The value C_{drw} = 34 µg/l has been calculated for local surface water and is used as drinking water value as a worst case scenario.

4.2 Effects on Human Health

4.2.1 Toxicokinetics, Metabolism and Distribution

1. Chemical Identity:

2-Methylbut-3-yn-2-ol has a high purity of 99.6 % [29].

2. Bioavailability:

2-Methylbut-3-yn-2-ol is miscible with water. The partition coefficient (log Pow) of 0.318 does not indicate a significant accumulation in biological tissues.

Relevant inhalatory exposure is possible due to its vapour pressure of 20 hPa at 20 °C.

3. Toxicokinetics and Metabolism:

There is no information on kinetics and metabolism from special studies. However, from the studies cited below it can be assumed that 2-Methylbut-3-yn-2-ol will be absorbed via the gastrointestinal tract and the respiratory tract. Dermal absorption must be low as no systemic toxicity was observed at a dose of 2,000 mg/kg b.w. while after acute oral exposure the LD_{50} in the same species is significantly lower (1,420 mg/kg b.w.).

4.2.2 Acute Toxicity

Animal data:

The acute oral toxicity was tested in rats with comparable results ranging from 1,300 to 2,600 mg/kg b.w. [13, 14, 15, 29]. Only from one study [13] details were available indicating a narcotic effect of 2-Methylbut-3-yn-2-ol, while the other studies were only quoted as secondary literature.

In mice the LD_{50} was reported to be between 500 [15] and 1,800 [17] mg/kg b.w. The inhalative LC_{50} (vapor) in rats was determined to be > 21.3 mg/l in a study in compliance with OECD

guideline 403 [18]. Local irritation and narcosis were noted during exposure only. In another study available as secondary literature the LC_{50} after 1-hour exposure in rats was > 20 mg/l [15]. The inhalation of a saturated atmosphere was not lethal to rats during the first 30 minutes of exposure and completely lethal within 4 hours of exposure indicating a narcotic effect [15]. In mice the LC_{50} was reported to be 2 mg/l/2h with no further details given [16]. The dermal LD_{50} in rats was above 2,000 mg/kg b.w. in a study in compliance with OECD guideline 402 [19]. No local irritation or signs of systemic toxicity were noted in rabbits who received 172 mg/kg b.w. on the shaven flank over 24 hours under occlusive conditions [13]. The intraperitoneal LD_{50} in mice was reported between 1,200 and 3,600 mg/kg b.w. [13, 20] while the subcutaneous LD_{50} in this species was 1,161 and 2,340 mg/kg b.w.**,** respectively [20, 21, 29].

Human experience: no data available.

Conclusion:

The available data are sufficient for initial hazard assessment. The data indicate that 2-Methylbut-3-yn-2-ol is harmful after oral exposure, however, no EU-classification is necessary with respect to inhalation and dermal exposure. High vapor concentrations can cause a narcotic effect as also seen after oral ingestion.

4.2.3 Irritation

Irritation/Corrosivity (animal tests):

2-Methylbut-3-yn-2-ol caused only a slight redness on the rabbit skin when applied full strength for 20 hours under occlusive conditions [13]. The compound was judged to be a severe irritant to the eye when rabbits received 50 µl into the conjunctival sac and staphyloma formation was noted 8 days after treatment indicating an irreversible effect [13]. A severe effect was also reported by another source where no detailed information was given [16].

Human experience: In single cases skin and eye irritation was reported after workers exposure to 2-Methylbut-3-yn-2-ol [28].

Conclusion:

The available data are sufficient for initial hazard assessment. 2-Methylbut-3-yn-2-ol is only a mild irritant after prolonged skin exposure and no classification is required taking EU criteria into consideration. However, 2-Methylbut-3-yn-2-ol is a severe eye irritant, thus classification with R 41 is necessary according to EU criteria.

4.2.4 Sensitization

Sensitization (animal tests):

In a modified Split Adjuvans Test guinea pigs received 0.1 ml 2-Methylbut-3-yn-2-ol four times on the shaven back while Freund's Complete Adjuvans was injected close to the application site after the 3rd treatment. The dermal challenge was performed 14 days later with 0.1 ml undiluted compound [22].

Human experience: no data available.

Conclusion:

The available data are sufficient for initial hazard assessment. There is no indication that 2-Methylbut-3-yn-2-ol is a skin sensitizer in guinea pigs.

4.2.5 Repeated Dose Toxicity

Animal data:

10 rats [BOR:WISW (SPF Cpb)] per sex and dose received 0, 50, 200 or 800 (after 3 days 600) mg/kg b.w. 2-Methylbut-3-yn-2-ol prepared in water to give a constant volume of 5 ml/kg over a period of 4 weeks by stomach tube [23].

Due to severe toxicity the highest dose was reduced to 600 mg/kg b.w. after 3 days. This dose was still toxic causing sedation, narcosis, hypothermia increased mortality. Food consumption was reduced and body weight development was retarded. Hematological examination at study termination revealed a statistically significant ($p \leq 0.05$) reduced number of leukocytes and hemoglobin concentration. No effects were noted for other hematological parameters such as number of thrombocytes, reticulocytes, MCV, MCH, MCHC and hematocrit. The differential blood count revealed a statistically significant increase ($p \leq 0.01$) in the ratio and number of polymorphonuclear neutrophiles at the high dose level while the ratio and number of lymphocytes was decreased (males also at 200 mg/kg b.w.). Polychromasia was increased dose dependent from 200 mg/kg b.w. onwards. An increase of anisocytosis was noted at 600 mg/kg b.w. for both sexes and 200 mg/kg b.w. for females only. The number of anulocytes was increased at the high dose level. Clinical chemistry at study termination revealed a statistically significant ($p \leq 0.05$) increase of GPT (glutamat-pyruvate transaminase) and cholesterol in both sexes at the high dose level and bilirubine and total protein was increased in females only. No clinical chemical changes were noted for the lower dose levels. Macroscopic and microscopic findings were restricted to high dose animals that died during the study indicating irritation of the upper gastrointestinal tract (hyperemia, focal bleeding, erosive/ulcerative gastritis). It is noteworthy that this was not observed in high dose animals which were treated throughout the whole study period making a substance related effect at 600 mg/kg b.w. less likely. A NOAEL was achieved at 50 mg/kg b.w. while a dose of 200 mg/kg b.w. represents a marginal toxic effect level when some minor hematological changes were noted.

Human data: no data available.

Conclusion:

The available data are sufficient for initial hazard assessment. A NOAEL of 50 mg/kg b.w. can be used for further calculation.

4.2.6 Mutagenicity

Bacterial systems:

2-Methylbut-3-yn-2-ol was not mutagenic in the Ames test when Salmonella typhimurium strains (TA 98, 100, 1535, 1537, 1538) were exposed up to 2,500 µl/plate with and without metabolic activation [25]. In another Ames test the same strains were treated with saturated vapors (51,721 ppm) of 2-Methylbut-3-yn-2-ol and no mutagenic effect was noted [24].

In vitro systems with mammalian cells: no data available.

In vivo systems with mammals:

2-Methylbut-3-yn-2-ol was also negative in the in vivo micronucleus test, when NMRI mice received 300, 600 or 1,200 mg/kg b.w. by i.p. injection [26]. There was no indication of any impairment of chromosome distribution in this study.
Conclusion:

The available data are sufficient for initial hazard assessment. 2-Methylbut-3-yn-2-ol is neither mutagenic in bacterial cells or animals when somatic cells were evaluated.

4.2.7 Carcinogenicity

No animal data available.

No information on potential human carcinogenicity is available.

4.2.8 Toxicity for Reproduction

Fertility: No data available

Developmental toxicity:

Female Wistar rats received 0, 45, 130 and 400 mg/kg b.w. 2-Methylbut-3-yn-2-ol by stomach tube from day 6 through 15 of gestation [27]. The study was performed in compliance with OECD guideline 414 and the dams were sacrificed on day 21 of the study. A dose of 400 mg/kg b.w. caused clinical symptoms (apathy, unsteady gait and/or piloerection) throughout the entire treatment period (shortly after test substance administration over a daily period of several hours). The clinical symptoms are in line with observations from a 28-day study and acute studies with 2-Methylbut-3-yn-2-ol [23]. In addition, transient (day 6 to 8 post coitum) reduced food consumption and body weight loss were noted for this dose group. No effects on the maternal organisms were found in the lower dose groups. Embryo-/fetotoxicity was noted only for the high dose group of 400 mg/kg b.w. Mean fetal weights were statistically significant reduced by about 6 %. The number of rudimentary cervical or accessory 14^{th} ribs were statistically significant increased as was the rate of fetuses showing skeletal retardations (poor or missing ossifications of the skull bones, thoracic vertebral bodies and/or sternebra). Thus the NOAEL for maternal and embryo-/fetotoxicity is 130 mg/kg b.w. No malformations were noted at any dose.

Human experience: no data available.

Conclusion:

The available data are sufficient for initial hazard assessment. 2-Methylbut-3-yn-2-ol is not a teratogen. Embryo-/fetotoxic effects were only noted at doses causing marked maternal toxicity (clinical symptoms). A NOAEL of 130 mg/kg b.w. can be used for further calculation.

4.2.9 Any Other Human Health Related Information that is available

Some additional information can be derived from older safety pharmacological studies [21, 14, 29]. A concentration of 0.67 mmol/l of 2-Methylbut-3-yn-2-ol (56.4 mg/ml) caused a 50 % hemolysis in vitro in human blood [21, 29]. In dog blood this value was 0.6 mmol/l (50.5 mg/l) [21, 29]. Slight sedative effects on CNS functions were noted in animals [21, 14, 29]. The ED50 for a lateral

position in mice was 780 mg/kg b.w. of 2-Methylbut-3-yn-2-ol after subcutaneous injection while this dose was 100 mg/kg b.w. for phenobarbital [21, 29]. A dose of 1,200 mg/kg b.w. 2-Methylbut-3-yn-2-ol caused after 5.8 minutes an average sleeping time of 275 minutes [21, 29]. For phenobarbital this value was 130 minutes after 115 mg/kg b.w. was injected 38 minutes before the animals fell asleep [21, 29]. The threshold of convulsion caused by Cardiazol was increased 1.9 times when mice received 700 mg/kg b.w. 2-Methylbut-3-yn-2-ol [21, 29]. An anticonvulsive effect was also noted in rats after electroshock treatment. The oral dose of 2-Methylbut-3-yn-2-ol was 140 mg/kg b.w. while the dose of phenobarbital was 19 mg/kg b.w. [14, 29].

Conclusion:

This information is not relevant for risk assessment as the observed effects on red blood cells and narcotic properties of 2-Methylbut-3-yn-2-ol have also been observed in animal studies cited above. These studies are more suitable for risk assessment as they take the kinetic properties and the metabolic transformation of the whole animal into account.

4.3 Risk Characterization

4.3.0 General Aspects

There is no information on kinetics and metabolism from special studies. However, from the studies cited below it can be assumed that 2-Methylbut-3-yn-2-ol will be absorbed via the gastrointestinal tract and the respiratory tract. Dermal absorption must be low as no systemic toxicity was observed at a dose of 2,000 mg/kg b.w. while after acute oral exposure the LD_{50} in the same species is significantly lower (1,420 mg/kg b.w.).

2-Methylbut-3-yn-2-ol is harmful after acute oral exposure and of low toxicity after dermal and inhalative exposure. High vapor concentrations can cause a narcotic effect as also seen after oral ingestion.

2-Methylbut-3-yn-2-ol is only a mild irritant after prolonged skin exposure. Severe damage to eyes was noted in animal studies. In some cases skin and eye irritation was reported in workers exposed to 2-Methylbut-3-yn-2-ol.

There is no indication that 2-Methylbut-3-yn-2-ol is a skin sensitizer in guinea pigs.

In a 4 week study with oral (gavage) exposure, a dose of 600 mg/kg b.w. was clearly toxic to rats causing sedation, narcosis, hypothermia, increased mortality, damage to red blood cells and liver, while there were only minor effects on red blood cells at the mid dose of 200 mg/kg b.w. and a NOAEL was achieved at 50 mg/kg b.w. 2-Methylbut-3-yn-2-ol was examined for prenatal toxicity up to 400 mg/kg b.w. and no malformations were noted. Embryo-/fetotoxic effects were only noted at the highest dose level of 400 mg/kg b.w. causing also marked maternal toxicity (clinical symptoms). A NOAEL of 130 mg/kg b.w. was achieved for maternal toxicity as well as embryo- and fetotoxicity.

2-Methylbut-3-yn-2-ol is neither mutagenic in bacterial cells or animals when somatic cells were evaluated.

There is no information on reproduction toxicity and carcinogenicity from animal studies. With the exception of occasional irritation to skin and eyes there is no information on human health effects.

4.3.1 Workers

From workplace measurements performed by BASF an exposure of 9.42 mg/m^3 has been calculated [30]. Assuming 100 % absorption, an inhaled air volume of 10 m^3/8h working day an estimated EHE for a 70 kg worker will be 94.2 mg 2-Methylbut-3-yn-2-ol / working day corresponding to 1.35 mg 2-Methylbut-3-yn-2-ol / kg b.w.
The limiting NOAEL from toxicity studies can be derived from the 4 week oral gavage study being 50 mg/kg b.w. and no specific toxic effects requiring a lower NOAEL were observed for 2-Methylbut-3-yn-2-ol.

The margin of safety (MOS) can be calculated as:

$$\frac{\text{NOAEL}}{\text{EHE}} = \frac{\text{50 mg/kg b.w.}}{\text{1.35 mg/kg b.w.}} = 37$$

4.3.2 Consumers

No consumer exposure is expected due to the low concentration (< 0.1 %) of 2-Methylbut-3-yn-2-ol in endproducts [30].

4.3.3 Man Exposed Indirectly via the Environment

Indirect exposure via the environment (i.e. drinking water and food) has been calculated according to the TGD model [31]. A daily uptake of 0.001 mg/kg b.w. has been calculated when a PEClocal of 34 µg/l was taken into consideration as worst case [31].

Taking the limiting NOAEL of 50 mg/kg b.w. from the subacute 4 week rat study into account the margin of safety is:

$$\frac{\text{50 mg/kg b.w.}}{\text{0.001 mg/kg b.w.}} = 50{,}000$$

5. Conclusions and Recommendations

5.1 Conclusions

The hazard assessment for the aquatic compartment showed that the calculated PEC/PNEC ratios are lower than 1. On the whole, 2-Methylbut-3-yn-2-ol is of low concern to this compartment.

Taking into account the systemic toxicity of 2-Methylbut-3-yn-2-ol, there is no reason for concern; the substance is of low potential risk and low priority for further work. The most sensitive NOAEL is derived from a 4 week oral gavage study in rats with a NOAEL of 50 mg/kg b.w. . Taking an EHE of 1.35 mg/kg/d for workers into account, there is a MOS of 37. Via the environment a daily uptake of 0.001 mg/kg b.w. was calculated giving a MOS of 50,000.

5.2 Recommendations

No further tests are needed.

6. Reference

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4.: OECD Initial Assessment Report: 3-Pyridinecarboxylic acid, CAS-No. 59-76-6, Phase I

5.: Veith G.D. et al. 1989: The toxicity of acetylenic alcohols to the fathead minnow, Pimephales promelas: narcosis and proelectrophile activation, Xenobiotica 19/5, 555-565

6.: BASF AG 1988a: unpublished data

7.: BASF AG 1988b: unpublished data

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13.: BASF AG 1966: unpublished data

14.: Brown B. et al.: J. Pharmacol. Exp. Ther. 115, 230-239 (1995), cited in: BG Chemie, Datenkatalog 205

15.: Air Products & Chemicals Inc., Allentown PA, USA (1975), cited in: HEDSET of Anchor Chemical (UK) Ltd., April 27, 1994

16.: Balynina E.S.: Gig Tr. Prof. Zabol. 31(4), 55 (1987)

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19.: Air Products & Chemicals Inc., Allentown PA, USA (1992), cited in: HEDSET of Anchor Chemical (UK) Ltd, April 27, 1994

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25.: BASF AG, Department of Toxicology, unpublished study (80/299), Dec. 12, 1980

26.: BASF AG, Department of Toxicology, unpublished data (26M0231/934206), Dec. 15, 1995

27.: BASF AG, Department of toxicology, unpublished data (93/231), Jan. 15, 1997

28.: BASF Medical Department, unpublished data

29.: BG Chemie, Datenkatalog Nr. 205, 1991

30.: BASF Department of Emission Control and Ecology, unpublished data (1997)

31.:Letter from Umweltbundesamt to BASF 27.5.1998

EXTRACT FROM IRPTC LEGAL FILES

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file: 17.01 LEGAL   rn : 523318
         !!! WARNING - not original IRPTC record - WARNING !!!
systematic name:3-Butyn-2-ol, 2-methyl-
common name    :dimethylethynylcarbinol
reported name  :2-Methyl-3-butyne-2-ol
cas no         :115-19-5            rtecs no       :ES0810000
area          : DEU                 type          : REG
 --------------------------------
|subject|specification|descriptor|
|-------+-------------+----------|
| AQ    |             |   CLASS  |
| USE   |    INDST    |   RQR    |
 --------------------------------
This substance is classified as moderately hazardous to water (Water
Hazard Class: WHC 1). (There are 3 water hazard classes: WHC 3 =
severely hazardous; WHC 2 = hazardous; WHC 1 = moderately hazardous; and
the classification as "not hazardous to water"). The purpose of the
classification is to identify the technical requirements of industrial
plants which handle substances hazardous to water.
entry date: SEP 2001                          effective date: 01JUN1999

title: Administrative Order relating to Substances Hazardous to Water
(Verwaltungsvorschrift wassergefaehrdende Stoffe)
original : BUANZ*, Bundesanzeiger, 51 , 98a , 1 , 1999


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file: 17.01 LEGAL   rn : 1105593
systematic name:3-Butyn-2-ol, 2-methyl-
common name    :dimethylethynylcarbinol
reported name  :dimethylethynylcarbinol
cas no         :115-19-5            rtecs no       :ES0810000
area          : RUS                 type          : REG
 --------------------------------
|subject|specification|descriptor|
|-------+-------------+----------|
| AIR   |    OCC      |   MAC    |
|       |             |   CLASS  |
 --------------------------------
CLV: 10MG/M3 (VAPOUR) HAZ. CLASS: III
entry date: MAY 1990                          effective date:   MAR1989

amendment: PDKAD*, PREDELNO DOPUSTIMYE KONTSENTRATSII VREDNYKH
           VESHCHESTV V VOZDUKHERABOCHEI ZONY (MAXIMUM ALLOWABLE
           CONCENTRATIONS OF HARMFUL SUBSTANCES IN OCCUPATIONAL AIR),
           4952-89 , , , 1989


                                *******


file: 17.01 LEGAL   rn : 1470471
         !!! WARNING - not original IRPTC record - WARNING !!!
systematic name:3-Butyn-2-ol, 2-methyl-
common name    :dimethylethynylcarbinol
reported name  :2-Methylbut-3-yn-2-ol
cas no         :115-19-5            rtecs no       :ES0810000
area          : EEC                 type          : REG
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subject	specification	descriptor
MANUF	INDST	CLASS
IMPRT	INDST	CLASS

The substance is included in a list of existing substances produced or imported within the Community in quantities exceeding 1000 tonnes per year. - A system of data reporting by any manufacturer who has produced or any importer who has imported the substance, as such or in a preparation, in quanities exceeding 10 tonnes per year is established.
entry date: AUG 1999 effective date: 04JUN1993

title: Council Regulation (EEC) No 793/93 of 23 March 1993 on the evaluation and control of the risks of existing substances
original : OJECFC, Official Journal of the European Communities, L84 , , 1 , 1993

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file: 17.01 LEGAL rn : 1660283
!!! WARNING - not original IRPTC record - WARNING !!!
systematic name:3-Butyn-2-ol, 2-methyl-
common name :dimethylethynylcarbinol
reported name :2-Methyl-2-hydroxy-3-butyne
cas no :115-19-5 rtecs no :ES0810000
area : IMO type : REG

subject	specification	descriptor
AQ	EMI	PRMT
TRNSP	MARIN	RQR

2-Methyl-2-hydroxy-3-butyne is designated as "III" in the Pollution Category Column of chapter 17 of the "International Bulk Chemical Code". - "III" means the product was evaluated and found to fall outside the Pollution Category A, B, C and D because the substances are at present considered to present no harm to human health, marine resources, amenities or other legitimate uses of the sea, when discharged into the sea from tank cleaning or deballasting operations. The substances are not subject to the provisions of Annex II of MARPOL 73/78.
entry date: JUN 1999 effective date: 03MCH1996

title: Regulations for the Control of Pollution by Noxious Liquid Substances in Bulk (Annex II of MARPOL 73/78)
original : MARPO*, International Convention for the Prevention of Pollution from Ships, 1973, as modified by the Protocol of 1978 relating thereto (MARPOL 73/78), Consolidated Edition, , , , 1997