

# I U C L I D

# D a t a s e t

Existing Chemical            Substance ID: 100-51-6  
CAS No.                      100-51-6  
EINECS Name                benzyl alcohol  
EINECS No.                 202-859-9  
Molecular Formula         C7H8O

Dataset created by:        EUROPEAN COMMISSION - European Chemicals Bureau

This dossier is a compilation based on data reported by the European Chemicals Industry following 'Council Regulation (EEC) No. 793/93 on the Evaluation and Control of the Risks of Existing Substances'. All (non-confidential) information from the single datasets, submitted in the IUCLID/HEDSET format by individual companies, was integrated to create this document.

The data have not undergone any evaluation by the European Commission.

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**1.0.1 OECD and Company Information**

**Name:** ANCHOR CHEMICAL(UK)LTD  
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**Country:** United Kingdom  
**Phone:** 061-223-2461  
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**Name:** Atochem  
**Street:** 4, Cours Michelet  
**Town:** 92080 Paris la Defense  
**Country:** France

**Name:** Bayer AG  
**Town:** 51368 Leverkusen  
**Country:** Germany

**Name:** CHEMAG Aktiengesellschaft  
**Town:** 60325 Frankfurt  
**Country:** Germany

**Name:** DSM Special Products B.V.  
**Street:** P.O. Box 602  
**Town:** 6160 MK Geleen  
**Country:** Netherlands  
**Phone:** 31 46 769222  
**Telefax:** 31 46 330112

**Name:** Tessenderlo Chemie  
**Street:** Industriepark Schoonhees-west, A 13 - E 313 AFRIT 25A,  
Stationstraat z/n  
**Town:** 3980 Tessenderlo  
**Country:** Belgium

**1.0.2 Location of Production Site**

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**1.0.3 Identity of Recipients**

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**1.1 General Substance Information**

**Substance type:** element  
**Physical status:** liquid

**Substance type:** organic  
**Physical status:** liquid

**1.1.1 Spectra**

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**1.2 Synonyms**

(Hydroxymethyl)Benzene

**Source:** DSM Special Products B.V. Geleen

ABY

**Source:** Atochem Paris la Defense

alfa-Hydroxytoluene

**Source:** DSM Special Products B.V. Geleen

alfa-Toluenol

**Source:** DSM Special Products B.V. Geleen  
Tessenderlo Chemie Tessenderlo

ALPHA-HYDROXYTOLUOL

**Source:** Bayer AG Leverkusen

ALPHA-OXYTOLUOL

**Source:** Bayer AG Leverkusen

Benzal alcohol

**Source:** Tessenderlo Chemie Tessenderlo

Benzenecarbinol

**Source:** Tessenderlo Chemie Tessenderlo

Benzenemethanol

**Source:** DSM Special Products B.V. Geleen

BENZENEMETHANOL

**Source:** Bayer AG Leverkusen

BENZOLCARBINOL

**Source:** Bayer AG Leverkusen

BENZOLMETHANOL

**Source:** Bayer AG Leverkusen

Benzoyl alcohol

**Source:** Tessenderlo Chemie Tessenderlo

Benzyl alcohol

**Source:** Tessenderlo Chemie Tessenderlo

BENZYL ALCOHOL

**Source:** ANCHOR CHEMICAL(UK)LTD MANCHESTER

BENZYLALKOHOL

**Source:** Bayer AG Leverkusen

## HYDROXYMETHYLBENZOL

**Source:** Bayer AG Leverkusen

## Hydroxytoluene

**Source:** Tessenderlo Chemie Tessenderlo

## methanol, Phenyl

**Source:** Tessenderlo Chemie Tessenderlo

## Phenolcarbinol

**Source:** Tessenderlo Chemie Tessenderlo

## Phenylcarbinol

**Source:** DSM Special Products B.V. Geleen

## PHENYLCARBINOL

**Source:** Bayer AG Leverkusen

## Phenylmethanol

**Source:** DSM Special Products B.V. Geleen

## PHENYLMETHANOL

**Source:** Bayer AG Leverkusen

## Phenylmethyl alcohol

**Source:** Tessenderlo Chemie Tessenderlo

## PHENYLMETHYLALKOHOL

**Source:** Bayer AG Leverkusen

**1.3 Impurities**

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**1.4 Additives**

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**1.5 Quantity**

**Quantity** 10 000 - 50 000 tonnes

**1.6.1 Labelling**

**Labelling:** as in Directive 67/548/EEC

**Symbols:** Xn

C

**Specific limits:** yes

**R-Phrases:** (20/22) Harmful by inhalation and if swallowed

**S-Phrases:** (2) Keep out of reach of children

(26) In case of contact with eyes, rinse immediately with plenty of water and seek medical advice

### 1.6.2 Classification

**Classification:** as in Directive 67/548/EEC  
**Class of danger:** corrosive  
**R-Phrases:** (20/22) Harmful by inhalation and if swallowed

### 1.7 Use Pattern

**Type:** type  
**Category:** Non dispersive use

**Type:** type  
**Category:** Use in closed system

**Type:** type  
**Category:** Use resulting in inclusion into or onto matrix

**Type:** type  
**Category:** Wide dispersive use

**Type:** industrial  
**Category:** Agricultural industry

**Type:** industrial  
**Category:** Basic industry: basic chemicals

**Type:** industrial  
**Category:** Chemical industry: used in synthesis

**Type:** industrial  
**Category:** Paints, lacquers and varnishes industry

**Type:** industrial  
**Category:** Paper, pulp and board industry

**Type:** industrial  
**Category:** Photographic industry

**Type:** industrial  
**Category:** Public domain

**Type:** industrial  
**Category:** Textile processing industry

**Type:** use  
**Category:** Adhesive, binding agents

**Type:** use  
**Category:** Cosmetics

**Type:** use  
**Category:** Food/foodstuff additives

**Type:** use  
**Category:** Intermediates

Type: use  
Category: Odour agents

Type: use  
Category: Pesticides

Type: use  
Category: Pharmaceuticals

Type: use  
Category: Photochemicals

Type: use  
Category: Process regulators

Type: use  
Category: Solvents

### 1.7.1 Technology Production/Use

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### 1.8 Occupational Exposure Limit Values

Type of limit: MAC (NL)  
Limit value:  
Remark: none  
Source: Tessenderlo Chemie Tessenderlo

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Type of limit: other  
Limit value: 5 other  
Remark: Provisional TLV (DSM-advice)  
5 ppm  
Source: DSM Special Products B.V. Geleen

Type of limit:  
Limit value:  
Remark: No data available on Occupational Exposure Limit Values  
Source: Atochem Paris la Defense

### 1.9 Source of Exposure

Remark: Benzaldehyde ---- H2 ----> Benzylalcohol  
Used in closed system  
No exposure  
Source: DSM Special Products B.V. Geleen

Remark: skin and inhalation  
Source: Tessenderlo Chemie Tessenderlo

**Remark:** Process :  
Reaction of alpha-chlorotoluene with Na<sub>2</sub>CO<sub>3</sub> in presence of Sodium hydroxide. Benzyl alcohol is obtained after purification by decantation and distillation.

EFFLUENTS & WASTES :

- During the reaction, carbon dioxide is produced. This gas is stripped to extract traces of organic compounds.
- Residues containing dibenzyle oxide, alpha-hydroxy (benzyl) toluene isomers and high molecular weight polymers are incinerated by an agreed incineration center.

**Source:** Atochem Paris la Defense

### **1.10.1 Recommendations/Precautionary Measures**

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### **1.10.2 Emergency Measures**

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### **1.11 Packaging**

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### **1.12 Possib. of Rendering Subst. Harmless**

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### **1.13 Statements Concerning Waste**

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### **1.14.1 Water Pollution**

**Classified by:** KBwS (DE)  
**Labelled by:** KBwS (DE)  
**Class of danger:** 1 (weakly water polluting)  
**Source:** Bayer AG Leverkusen

**Classified by:**  
**Labelled by:**  
**Class of danger:** 1 (weakly water polluting)  
**Source:** CHEMAG Aktiengesellschaft Frankfurt

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### **1.14.2 Major Accident Hazards**

**Legislation:**  
**Substance listed:** no  
**Source:** Bayer AG Leverkusen

### **1.14.3 Air Pollution**

**Classified by:** other: Bayer AG  
**Labelled by:** other: Bayer AG  
**Number:** 3.1.7 (organic substances)  
**Class of danger:** III  
**Source:** Bayer AG Leverkusen

### **1.15 Additional Remarks**

**Remark:** Disposal : Combustion in an incinerator for chemical waste according national and local regulations

Product is offered in bulk and drums

Transport information: RID: 3/32C  
ADR: 3/32C

**Source:** For any transport by air, sea or inland waterways  
DSM Special Products B.V. Geleen

**Remark:** no additional remarks  
**Source:** Tessenderlo Chemie Tessenderlo

### **1.16 Last Literature Search**

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### **1.17 Reviews**

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### **1.18 Listings e.g. Chemical Inventories**

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**2.1 Melting Point**

**Value:** -15.3 degree C  
**Source:** Bayer AG Leverkusen (3)

**2.2 Boiling Point**

**Value:** 205.4 degree C at 1013 hPa  
**Source:** Bayer AG Leverkusen (3)

**2.3 Density**

**Type:** density  
**Value:** 1.0442 g/cm<sup>3</sup> at 22.5 degree C  
**Source:** Bayer AG Leverkusen (3)

**2.3.1 Granulometry**

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**2.4 Vapour Pressure**

**Value:** .03 hPa at 20 degree C  
**Source:** Bayer AG Leverkusen (3)

**Value:** .09 hPa at 30 degree C  
**Source:** Bayer AG Leverkusen (3)

**Value:** .67 hPa at 50 degree C  
**Source:** Bayer AG Leverkusen (3)

**2.5 Partition Coefficient**

**log Pow:** 1.1  
**Method:** other (calculated): Leo, A.: CLOGP-3.54 MedChem Software 1989.  
Daylight, Chemical Information Systems, Claremont, CA 91711,  
USA  
**Year:**  
**Source:** Bayer AG Leverkusen (4)

**log Pow:** 1.1  
**Method:**  
**Year:**  
**Remark:** experimentally determined  
**Source:** Bayer AG Leverkusen (5)

### 2.6.1 Water Solubility

**Value:** 40 g/l at 20 degree C  
**Source:** Bayer AG Leverkusen (6)

**Value:** 44 g/l at 50 degree C  
**Source:** Bayer AG Leverkusen (6)

### 2.6.2 Surface Tension

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### 2.7 Flash Point

**Value:** 101 degree C  
**Type:** closed cup  
**Method:** other: DIN 51758  
**Year:**  
**Source:** Bayer AG Leverkusen (6)

### 2.8 Auto Flammability

**Value:**  
**Remark:** ignition temperature: 435 degree C  
**Source:** Bayer AG Leverkusen (3)

### 2.9 Flammability

-

### 2.10 Explosive Properties

**Result:** other: explosive limits: lower 1.3 % by vol., upper 13.0 % by vol. at 170 degree C and 1.013 bar  
**Source:** Bayer AG Leverkusen (3)

### 2.11 Oxidizing Properties

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**2.12 Additional Remarks**

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**3.1.1 Photodegradation**

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**3.1.2 Stability in Water**

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**3.1.3 Stability in Soil**

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**3.2 Monitoring Data (Environment)**

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**3.3.1 Transport between Environmental Compartments**

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**3.3.2 Distribution**

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**3.4 Mode of Degradation in Actual Use**

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**3.5 Biodegradation**

**Type:** aerobic  
**Inoculum:** predominantly domestic sewage  
**Degradation:** > 90 % after 30 day  
**Method:** OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"  
**Year:** 1972 **GLP:** no  
**Test substance:**  
**Remark:** related to BOD  
**Source:** Bayer AG Leverkusen

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**Type:** aerobic  
**Inoculum:**  
**Degradation:** 62 % after 5 day  
**Method:** OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"  
**Year:** **GLP:** no  
**Test substance:**  
**Remark:** related to ThOD  
**Source:** Bayer AG Leverkusen

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**Type:** aerobic  
**Inoculum:**  
**Degradation:** 77 % after 20 day  
**Method:** OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"  
**Year:** **GLP:** no  
**Test substance:**  
**Remark:** related to ThOD  
**Source:** Bayer AG Leverkusen

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**Type:** aerobic  
**Inoculum:** activated sludge, adapted  
**Degradation:** 95 % after 28 day  
**Method:** other: Closed bottle test  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Test concentration: 2 - 5 mg/l  
Degradation related to ThOD  
**Source:** Bayer AG Leverkusen

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**Type:** aerobic  
**Inoculum:** domestic sewage  
**Degradation:** 89.2 % after 5 day  
**Method:** other: respirometric diluting method  
**Year:** **GLP:** no  
**Test substance:**  
**Remark:** related to ThOD  
**Source:** Bayer AG Leverkusen

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**Type:** aerobic  
**Inoculum:** activated sludge  
**Concentration:** 100 mg/l  
**Degradation:** 92 - 96 % after 28 day  
**Method:** other: see remarks  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Method: "Biodegradation test of chemical substance by micro-organisms etc." stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, the Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "301C, Ready Biodegradability: Modified MITI Test I" stipulated in the OECD Guidelines for Testing of Chemicals (May 12, 1981).  
sludge conc.: 30 mg/l  
**Source:** Bayer AG Leverkusen

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**Type:** aerobic  
**Inoculum:**  
**Degradation:** 85 % after 5 day  
**Method:**  
**Year:** **GLP:** no  
**Test substance:**  
**Remark:** related to ThOD  
**Source:** Bayer AG Leverkusen (12)

**Type:** anaerobic  
**Inoculum:** anaerobic sludge  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** 100 % mineralisation in 1 week (CH<sub>4</sub>-Production)  
**Source:** Bayer AG Leverkusen (13)

**Type:**  
**Inoculum:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** The activity of degradation is at a concentration of 100 mg/l not hindered in a model plant (Ascomat)  
**Source:** Bayer AG Leverkusen (7)

**Type:**  
**Inoculum:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Biodegradation characteristics: biodegraded completely in a short time by general microorganisms.  
**Source:** Bayer AG Leverkusen (14)

### **3.6 BOD<sub>5</sub>, COD or BOD<sub>5</sub>/COD Ratio**

**Remark:** ThOD: 2515.1 mg/l  
**Source:** Bayer AG Leverkusen (10)

### **3.7 Bioaccumulation**

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### **3.8 Additional Remarks**

**Remark:** ThOD 2520 mg/g  
COD 2520 mg/g  
BOD5 1560 mg/g  
Influence on biological purification plants:  
adapted 1180 mg/l degradable

**Source:** Bayer AG Leverkusen

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**AQUATIC ORGANISMS****4.1 Acute/Prolonged Toxicity to Fish**

**Type:** static  
**Species:** Leuciscus idus (Fish, fresh water)  
**Exposure period:** 48 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**LC0:** 630  
**LC50:** 646  
**Method:** other: Bestimmung der Wirkung von Wasserinhaltsstoffen auf Fische, DIN 38412 Teil 15  
**Year:** **GLP:** no  
**Test substance:**  
**Source:** Bayer AG Leverkusen (16)

**Type:** static  
**Species:** Petromyzon marinus  
**Exposure period:** 24 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**LC50:** >= 5  
**Method:**  
**Year:** **GLP:** no  
**Test substance:**  
**Remark:** larvae; screening test  
**Source:** Bayer AG Leverkusen (17)

**Type:**  
**Species:** Carassius auratus (Fish, fresh water)  
**Exposure period:** 24 hour(s)  
**Unit:** mg/l **Analytical monitoring:**  
**LC0:** >= 5  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (18)

**Type:**  
**Species:** Cyprinus carpio (Fish, fresh water)  
**Exposure period:** 48 hour(s)  
**Unit:** **Analytical monitoring:** no  
**LC0:** 136  
**Method:**  
**Year:** **GLP:** no  
**Test substance:**  
**Remark:** Testing of acute oral toxicity  
Unit: mg/kg  
**Source:** Bayer AG Leverkusen (19)

**Type:**  
**Species:** Lepomis macrochirus (Fish, fresh water)  
**Exposure period:** 24 hour(s)  
**Unit:** mg/l **Analytical monitoring:**  
**LC0:** >= 5  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (18)

**Type:**  
**Species:** Lepomis macrochirus (Fish, fresh water)  
**Exposure period:** 96 hour(s)  
**Unit:** mg/l **Analytical monitoring:**  
**LC50:** 10  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (20)

**Type:**  
**Species:** Menidia beryllina (Fish, estuary, marine)  
**Exposure period:** 96 hour(s)  
**Unit:** mg/l **Analytical monitoring:**  
**LC50:** 15  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (20)

**Type:**  
**Species:** Pimephales promelas (Fish, fresh water)  
**Exposure period:** 96 hour(s)  
**Unit:** mg/l **Analytical monitoring:**  
**LC50:** 460  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (21)

**Type:**  
**Species:** Salmo trutta (Fish, fresh water, marine)  
**Exposure period:** 24 hour(s)  
**Unit:** mg/l **Analytical monitoring:**  
**LC0:** >= 5  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (18)

**4.2 Acute Toxicity to Aquatic Invertebrates**

**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 24 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**EC0:** 300  
**EC50:** 400  
**Method:** other: Daphnien-Kurzzeitest, DIN 38412 Teil 11, Bestimmung der Wirkung von Wasserinhaltsstoffen auf Kleinkrebse  
**Year:** **GLP:** no  
**Test substance:**  
**Source:** Bayer AG Leverkusen (16)

**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 48 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**TGK :** 360  
**Method:** other: acute immobilisation test  
**Year:** **GLP:** no  
**Test substance:**  
**Source:** Bayer AG Leverkusen (22)

**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 24 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**EC0:** 26  
**EC50:** 55  
**EC100:** 100  
**Method:**  
**Year:** **GLP:** no  
**Test substance:**  
**Source:** Bayer AG Leverkusen (23)

**4.3 Toxicity to Aquatic Plants e.g. Algae**

**Species:** Anabaena cylindrica (Algae)  
**Endpoint:**  
**Exposure period:** 3 hour(s)  
**Unit:** mg/l **Analytical monitoring:**  
**EC50:** 90  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** blue-green algae  
Inhibition of photosynthesis  
**Source:** Bayer AG Leverkusen (24)

**Species:** Anabaena inaequalis (Algae)  
**Endpoint:**  
**Exposure period:** 3 hour(s)  
**Unit:** mg/l **Analytical monitoring:**  
**EC0:** 30  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** blue-green algae  
Inhibition of photosynthesis  
**Source:** Bayer AG Leverkusen (24)

**Species:** Anabaena variabilis (Algae)  
**Endpoint:**  
**Exposure period:** 3 hour(s)  
**Unit:** mg/l **Analytical monitoring:**  
**EC50:** 35  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** blue-green algae  
Inhibition of photosynthesis  
**Source:** Bayer AG Leverkusen (24)

**Species:** Chlorella pyrenoidosa (Algae)  
**Endpoint:**  
**Exposure period:** 3 hour(s)  
**Unit:** mg/l **Analytical monitoring:**  
**EC50:** 95  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** green algae  
Inhibition of photosynthesis  
**Source:** Bayer AG Leverkusen (24)

**Species:** Haematococcus pluvialis (Algae)  
**Endpoint:**  
**Exposure period:** 4 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**EC50:** 2600  
**Method:** other: Verfahren nach Tuempling im Warburgapparat  
**Year:** **GLP:** no  
**Test substance:**  
**Source:** Bayer AG Leverkusen (16)

**Species:** Scenedesmus quadricauda (Algae)  
**Endpoint:**  
**Exposure period:** 96 hour(s)  
**Unit:** mg/l **Analytical monitoring:**  
**TGK :** 640  
**Method:** other: cell multiplication inhibition test  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** green algae  
**Source:** Bayer AG Leverkusen (22)

**Species:** Scenedesmus quadricauda (Algae)  
**Endpoint:**  
**Exposure period:** 3 hour(s)  
**Unit:** mg/l **Analytical monitoring:**  
**EC50:** 79  
**Method:**  
**Year:** **GLP:** no  
**Test substance:**  
**Remark:** green algae  
 Inhibition of photosynthesis  
**Source:** Bayer AG Leverkusen (24)

#### 4.4 Toxicity to Microorganisms e.g. Bacteria

**Type:** aquatic  
**Species:** Escherichia coli (Bacteria)  
**Exposure period:** 48 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**EC0:** 1000  
**Method:** other: cell multiplication test  
**Year:** **GLP:** no  
**Test substance:**  
**Source:** Bayer AG Leverkusen (22)

**Type:** aquatic  
**Species:** Photobacterium phosphoreum (Bacteria)  
**Exposure period:** 30 minute(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**EC50:** 71.42  
**Method:** other: Microtox  
**Year:** **GLP:** no  
**Test substance:**  
**Source:** Bayer AG Leverkusen (25)

**Type:** aquatic  
**Species:** Photobacterium phosphoreum (Bacteria)  
**Exposure period:** 5 minute(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**EC50:** 50  
**Method:**  
**Year:** **GLP:** no  
**Test substance:**  
**Source:** Bayer AG Leverkusen (26)

**Type:** aquatic  
**Species:** Pseudomonas putida (Bacteria)  
**Exposure period:**  
**Unit:** mg/l **Analytical monitoring:** no  
**EC10:** 658  
**Method:** other: Test according to Bringmann and Kuehn (cell multiplication inhibition test)  
**Year:** **GLP:** no  
**Test substance:**  
**Remark:** Exposure period: 16-18 h  
**Source:** Bayer AG Leverkusen (16)

**Type:** aquatic  
**Species:** other bacteria: Aerobic heterotrophic  
**Exposure period:** 49 hour(s)  
**Unit:** mg/l **Analytical monitoring:**  
**IC50 :** 2100  
**Method:**  
**Year:** **GLP:** no  
**Test substance:**  
**Remark:** Inhibition of respiration;  
prolonged incubation compared with ISO 8192  
**Source:** Bayer AG Leverkusen (27)

**Type:** aquatic  
**Species:** other bacteria: Nitrosomonas  
**Exposure period:** 24 hour(s)  
**Unit:** mg/l **Analytical monitoring:**  
**IC50 :** 390  
**Method:** other: Inhibition of nitrification, comparable with ISO/DIS 9509  
**Year:** **GLP:** no  
**Test substance:**  
**Remark:** Inhibition of N-oxidation  
**Source:** Bayer AG Leverkusen (27)

**4.5 Chronic Toxicity to Aquatic Organisms****4.5.1 Chronic Toxicity to Fish**

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**4.5.2 Chronic Toxicity to Aquatic Invertebrates**

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**TERRESTRIAL ORGANISMS****4.6.1 Toxicity to Soil Dwelling Organisms**

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**4.6.2 Toxicity to Terrestrial Plants**

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**4.6.3 Toxicity to other Non-Mamm. Terrestrial Species**

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**4.7 Biological Effects Monitoring**

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**4.8 Biotransformation and Kinetics**

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**4.9 Additional Remarks**

<b>Remark:</b>	Aedes aegypti, eggs	(72h)	LD50	160	l/ha
			LD90	251	l/ha
	Aedes aegypti, larval stage L1	(24h)	LD50	105	l/ha
			LD90	132	l/ha
	Aedes aegypti, larval stage L3-L4	(24h)	LD50	129	l/ha
			LD90	184	l/ha
	Aedes scutellaris, eggs	(72h)	LD50	160	l/ha
			LD90	265	l/ha
	Aedes scutellaris, larval stage L1	(24h)	LD50	110	l/ha
			LD90	151	l/ha
	Aedes scutellaris, larval stage L3-L4	(24h)	LD50	126	l/ha
			LD90	172	l/ha
<b>Source:</b>	Bayer AG Leverkusen				

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**5.1 Acute Toxicity****5.1.1 Acute Oral Toxicity**

Type: LD50  
Species: rat  
Sex:  
Number of  
Animals:  
Vehicle:  
Value: = 1610 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Remark: sex: male  
Source: Bayer AG Leverkusen (29)

Type: LD50  
Species: rat  
Sex:  
Number of  
Animals:  
Vehicle:  
Value: = 1230 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (30)

Type: LD50  
Species: rat  
Sex:  
Number of  
Animals:  
Vehicle:  
Value: = 2080 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (31) (32)

Type: LD50  
Species: rat  
Sex:  
Number of  
Animals:  
Vehicle:  
Value: = 3100 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (33)

Type: LDLo  
Species: rat  
Sex:  
Number of  
Animals:  
Vehicle:  
Value: ca. 1040 - 3120 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (34)

Type: LD50  
Species: mouse  
Sex:  
Number of  
Animals:  
Vehicle:  
Value: = 1580 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (30)

Type: LD50  
Species: mouse  
Sex:  
Number of  
Animals:  
Vehicle:  
Value: = 1150 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (35)

Type: LDLo  
Species: mouse  
Sex:  
Number of  
Animals:  
Vehicle:  
Value: ca. 1040 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (34)

Type: LD50  
Species: rabbit  
Sex:  
Number of  
Animals:  
Vehicle:  
Value: = 1040 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (31)

Type: LDLo  
Species: guinea pig  
Sex:  
Number of  
Animals:  
Vehicle:  
Value: ca. 1040 - 2600 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (34)

### 5.1.2 Acute Inhalation Toxicity

Type: LC50  
Species: rat  
Sex:  
Number of  
Animals:  
Vehicle:  
Exposure time: 4 hour(s)  
Value: > 4.178 mg/l  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (36)

Type: LC50  
Species: rat  
Sex:  
Number of  
Animals:  
Vehicle:  
Exposure time: 4 hour(s)  
Value: ca. 8.8 mg/l  
Method:  
Year: GLP:  
Test substance:  
Remark: Extrapolation according to Haber's law: LC50 (8h) = 1000 ppm.  
Source: Bayer AG Leverkusen

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Type: LC50  
Species: rat  
Sex:  
Number of  
Animals:  
Vehicle:  
Exposure time: 4 hour(s)  
Value: > .9 mg/l  
Method:  
Year: GLP:  
Test substance:  
Remark: LC33 (4h) = 200 ppm.  
Source: Bayer AG Leverkusen

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### 5.1.3 Acute Dermal Toxicity

Type: LD50  
Species: rabbit  
Sex:  
Number of  
Animals:  
Vehicle:  
Value: = 2000 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen

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Type: LD50  
Species: guinea pig  
Sex:  
Number of  
Animals:  
Vehicle:  
Value: < 5000 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen

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**5.1.4 Acute Toxicity, other Routes**

**Type:** LD50  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Route of admin.:** i.p.  
**Value:** > 400 - 800 mg/kg bw  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (32)

**Type:** LD50  
**Species:** mouse  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Route of admin.:** i.p.  
**Value:** = 1000 mg/kg bw  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Sex: male  
Strain: CD-1  
Acute toxicity after 4 h.  
**Source:** Bayer AG Leverkusen (39)

**Type:** LD50  
**Species:** mouse  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Route of admin.:** i.p.  
**Value:** = 650 mg/kg bw  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Sex: male  
Strain: CD-1  
Acute delayed toxicity after 7 d.  
**Source:** Bayer AG Leverkusen (39)

## 5. Toxicity

date: 18-FEB-2000  
Substance ID: 100-51-6

Type: LD50  
Species: guinea pig  
Sex:  
Number of  
Animals:  
Vehicle:  
Route of admin.: i.p.  
Value: > 400 - 800 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (32)

Type: LD50  
Species: rat  
Sex:  
Number of  
Animals:  
Vehicle:  
Route of admin.: s.c.  
Value: = 1700 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (40)

Type: LD50  
Species: mouse  
Sex:  
Number of  
Animals:  
Vehicle:  
Route of admin.: s.c.  
Value: = 950 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (35)

Type: other: LDLO  
Species: rabbit  
Sex:  
Number of  
Animals:  
Vehicle:  
Route of admin.: s.c.  
Value: ca. 2080 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (34)

Type: LD50  
Species: rat  
Sex:  
Number of  
Animals:  
Vehicle:  
Route of admin.: i.v.  
Value: = 314 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (41)

Type: LD50  
Species: rat  
Sex:  
Number of  
Animals:  
Vehicle:  
Route of admin.: i.v.  
Value: = 53 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Remark: Rapid injection  
Source: Bayer AG Leverkusen (41)

Type: LD50  
Species: mouse  
Sex:  
Number of  
Animals:  
Vehicle:  
Route of admin.: i.v.  
Value: = 324 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (42)

Type: LD50  
Species: mouse  
Sex:  
Number of  
Animals:  
Vehicle:  
Route of admin.: i.v.  
Value: ca. 105 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Remark: LD50 value depends on speed of injection  
Source: Bayer AG Leverkusen (43)

Type: LD50  
Species: mouse  
Sex:  
Number of  
Animals:  
Vehicle:  
Route of admin.: i.v.  
Value: = 1460 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (41)

Type: other: LDLO  
Species: mouse  
Sex:  
Number of  
Animals:  
Vehicle:  
Route of admin.: i.v.  
Value: ca. 135 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Remark: sex: male; strain: CD-1  
Source: Bayer AG Leverkusen (44)

Type: other: LDLO  
Species: dog  
Sex:  
Number of  
Animals:  
Vehicle:  
Route of admin.: i.v.  
Value: ca. 50 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (41)

Type: LD50  
Species: rat  
Sex:  
Number of  
Animals:  
Vehicle:  
Route of admin.: other  
Value: = 410 mg/kg bw  
Method:  
Year: GLP:  
Test substance:  
Remark: Application: intra-arterial.  
Source: Bayer AG Leverkusen (41)

## 5.2 Corrosiveness and Irritation

### 5.2.1 Skin Irritation

Species: rabbit  
Concentration:

Exposure:  
Exposure Time:  
Number of  
Animals:  
PDII:  
Result: not irritating  
EC classificat.:  
Method: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen (43)

Species: rabbit  
Concentration:

Exposure:  
Exposure Time:  
Number of  
Animals:  
PDII:  
Result: slightly irritating  
EC classificat.:  
Method: other: see remarks  
Year: GLP:  
Test substance:  
Remark: Exposure time: 24 h, dose: 10 mg, no other data.  
Source: Bayer AG Leverkusen (40) (33)

Species: rabbit  
Concentration:

Exposure:  
Exposure Time:  
Number of  
Animals:  
PDII:  
Result: moderately irritating  
EC classificat.:  
Method: other: see remarks  
Year: GLP:  
Test substance:  
Remark: Exposure time: 24 h, clipped skin, 100 mg/animal, open,  
observation time: 72 h.  
Source: Bayer AG Leverkusen (45)

**Species:** rabbit  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of Animals:**  
**PDII:**  
**Result:** not irritating  
**EC classificat.:**  
**Method:** other: see remarks  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Exposure time: 24 h, ear, ca. 500 mg/animal, semi-occlusive, observation time: 7 d.  
**Source:** Bayer AG Leverkusen

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**Species:** guinea pig  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of Animals:**  
**PDII:**  
**Result:** moderately irritating  
**EC classificat.:**  
**Method:** other: see remarks  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Exposure time: 24 h, depilated skin, dose: undiluted material, no other data, open, observation time: no data.  
**Source:** Bayer AG Leverkusen

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**Species:** guinea pig  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of Animals:**  
**PDII:**  
**Result:** slightly irritating  
**EC classificat.:**  
**Method:** other: see remarks  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Exposure time: 24 h, clipped flank, dose: 8 mg/animal (30 % in unspecified solvent), open, observation time: no data.  
**Source:** Bayer AG Leverkusen

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**Species:** guinea pig  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of Animals:**  
**PDII:**  
**Result:** slightly irritating  
**EC classificat.:**  
**Method:** other: see remarks  
**Year:** **GLP:**

**Test substance:**  
**Remark:** Exposure time: 24 h, shaved flanks, dose: 26 mg/animal (25 % unspecified solvent), intradermally, observation time: no data.  
**Source:** Bayer AG Leverkusen (48)

**Species:** guinea pig  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of Animals:**  
**PDII:**  
**Result:** not irritating  
**EC classificat.:**  
**Method:** other: see remarks  
**Year:** **GLP:**

**Test substance:**  
**Remark:** Exposure time: 24 h, clipped skin, 100 mg/animal, open, observation time: 72 h.  
**Source:** Bayer AG Leverkusen (45)

**Species:** human  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of Animals:**  
**PDII:**  
**Result:** irritating  
**EC classificat.:**  
**Method:** other: Closed Patch Test  
**Year:** **GLP:**

**Test substance:**  
**Remark:** Observation time: 24/48 h, 0.05 % in either ethanol or a cream base produced irritation in 18 of 614 subjects.  
**Source:** Bayer AG Leverkusen (49)

**Species:** human  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of Animals:**  
**PDII:**  
**Result:** irritating  
**EC classificat.:**  
**Method:** other: Uncovered Patch Test  
**Year:** **GLP:**

**Test substance:**  
**Remark:** 0.5 % in petrolatum induced contact urticaria in 7 of 32 volunteers.  
**Source:** Bayer AG Leverkusen

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**Species:** human  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of Animals:**  
**PDII:**  
**Result:** slightly irritating  
**EC classificat.:**  
**Method:** other: Patch Test  
**Year:** **GLP:**

**Test substance:**  
**Remark:** Exposure time: 48 h, ca. 50 mg/person (30 % in acetone), observation time: up to 120 h.  
**Source:** Bayer AG Leverkusen

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**Species:** other: Male nude mouse  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of Animals:**  
**PDII:**  
**Result:** highly irritating  
**EC classificat.:**  
**Method:** other: see remarks  
**Year:** **GLP:**

**Test substance:**  
**Remark:** Exposure time: 24 h, 10 % in purified water, occlusive, observation time: no data.  
**Source:** Bayer AG Leverkusen

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**Species:** other: mini-pig  
**Concentration:**  
**Exposure:**  
**Exposure Time:**  
**Number of Animals:**  
**PDII:**  
**Result:** not irritating  
**EC classificat.:**  
**Method:** other: Patch Test  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Exposure time: 48 h, clipped skin, 50 mg/animal, observation time: no data.  
**Source:** Bayer AG Leverkusen

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### 5.2.2 Eye Irritation

**Species:** rabbit  
**Concentration:**  
**Dose:**  
**Exposure Time:**  
**Comment:**  
**Number of Animals:**  
**Result:** moderately irritating  
**EC classificat.:**  
**Method:** OECD Guide-line 405 "Acute Eye Irritation/Corrosion"  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen

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**Species:** rabbit  
**Concentration:**  
**Dose:**  
**Exposure Time:**  
**Comment:**  
**Number of Animals:**  
**Result:** highly irritating  
**EC classificat.:**  
**Method:** other: see remarks  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Exposure time: 24 h, dose: 750 microg., no other data.  
**Source:** Bayer AG Leverkusen

(40) (33)

Species: rabbit  
Concentration:  
Dose:  
Exposure Time:  
Comment:  
Number of  
Animals:  
Result: not irritating  
EC classificat.:  
Method: other: see remarks  
Year: GLP:  
Test substance:  
Remark: 4 % aqueous solution, tested for stability, no other data.  
Source: Bayer AG Leverkusen (52)

Species: rabbit  
Concentration:  
Dose:  
Exposure Time:  
Comment:  
Number of  
Animals:  
Result: not irritating  
EC classificat.:  
Method: other: see remarks  
Year: GLP:  
Test substance:  
Remark: Exposure time: 4 d, 2 drops of a 0.08 % aqueous solution,  
no other data.  
Source: Bayer AG Leverkusen (35)

Species: rabbit  
Concentration:  
Dose:  
Exposure Time:  
Comment:  
Number of  
Animals:  
Result: moderately irritating  
EC classificat.:  
Method: other: see remarks  
Year: GLP:  
Test substance:  
Remark: ca. 100 mg/animal, observation time: 7 d.  
Source: Bayer AG Leverkusen (46)

**5.3 Sensitization**

**Type:** Draize Test  
**Species:** guinea pig  
**Number of Animals:**  
**Vehicle:**  
**Result:** not sensitizing  
**Classification:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (47)

**Type:** Freund's complete adjuvant test  
**Species:** guinea pig  
**Number of Animals:**  
**Vehicle:**  
**Result:** sensitizing  
**Classification:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (47)

**Type:** Guinea pig maximization test  
**Species:** guinea pig  
**Number of Animals:**  
**Vehicle:**  
**Result:** not sensitizing  
**Classification:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (47)

**Type:** Open epicutaneous test  
**Species:** guinea pig  
**Number of Animals:**  
**Vehicle:**  
**Result:** sensitizing  
**Classification:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (47)

**Type:** Patch-Test  
**Species:** human  
**Number of Animals:**  
**Vehicle:**  
**Result:** sensitizing  
**Classification:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (53) (54)

**Type:** Patch-Test  
**Species:** human  
**Number of Animals:**  
**Vehicle:**  
**Result:** ambiguous  
**Classification:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (50)

**Type:** Patch-Test  
**Species:** human  
**Number of Animals:**  
**Vehicle:**  
**Result:** sensitizing  
**Classification:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Maximum incidence of sensitization: 1 %.  
**Source:** Bayer AG Leverkusen (55) (56) (57)

**Type:** Patch-Test  
**Species:** human  
**Number of Animals:**  
**Vehicle:**  
**Result:**  
**Classification:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Two patients with contact dermatitis were found to be sensitised by benzyl alcohol: 1 per cent in petrolatum  
**Source:** Bayer AG Leverkusen (58)

**Type:** Patch-Test  
**Species:** human  
**Number of Animals:**  
**Vehicle:**  
**Result:**  
**Classification:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** A previously to balsam of Peru sensitised patient reacted on patch testing with benzyl alcohol: 0.5 per cent in olive oil.  
**Source:** Bayer AG Leverkusen (59)

**Type:** other  
**Species:** laboratory animal  
**Number of Animals:**  
**Vehicle:**  
**Result:**  
**Classification:**  
**Method:** other: additional animal studies are reported  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (60) (61) (62) (63)

**Type:** other  
**Species:** human  
**Number of Animals:**  
**Vehicle:**  
**Result:**  
**Classification:**  
**Method:** other: additional data  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen  
 (64) (65) (66) (67) (68) (69) (70) (71) (72) (73) (74) (75) (76) (77)  
 (78) (79) (80) (81) (82) (83) (84) (85) (86) (87) (88) (89)

**Type:** other: Application to shaved skin  
**Species:** guinea pig  
**Number of Animals:**  
**Vehicle:**  
**Result:** not sensitizing  
**Classification:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (35)

**Type:** other: Intradermal application  
**Species:** guinea pig  
**Number of Animals:**  
**Vehicle:**  
**Result:** not sensitizing  
**Classification:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (35)

**Type:** other: Maximization Test  
**Species:** human  
**Number of Animals:**  
**Vehicle:**  
**Result:** not sensitizing  
**Classification:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (90)

#### **5.4 Repeated Dose Toxicity**

**Species:** rat **Sex:** male  
**Strain:** no data  
**Route of admin.:** inhalation  
**Exposure period:** no data  
**Frequency of treatment:** 4 h/d  
**Post. obs. period:** no data specified  
**Doses:** 216-270 ppm  
**Control Group:** no data specified  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** No. of animals: 6.  
**Result:** Subacute exposure to male rats for 4 h periods produced no clinical or pathologic signs of toxicity.  
**Source:** Bayer AG Leverkusen (37)

## 5. Toxicity

date: 18-FEB-2000  
Substance ID: 100-51-6

**Species:** rat **Sex:** male/female  
**Strain:** Sherman  
**Route of admin.:** inhalation  
**Exposure period:** 1 d  
**Frequency of treatment:** 4 h/d  
**Post. obs. period:** 14 d  
**Doses:** 2000 ppm = 8.9 mg/l  
**Control Group:** no  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** No. of animals: 6.  
**Result:** Exposure to 2000 ppm kills either 2/6, 3/6 or 4/6 rats. Therefore benzyl alcohol is considered to be of moderate toxicity.  
**Source:** Bayer AG Leverkusen

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**Species:** rat **Sex:** male/female  
**Strain:** other: F344/N  
**Route of admin.:** gavage  
**Exposure period:** 16 d  
**Frequency of treatment:** daily  
**Post. obs. period:** no  
**Doses:** 125, 250, 500, 1000, 2000 mg/kg/d  
**Control Group:** no data specified  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** No. of animals: 5/sex/dose.  
**Result:** All male and female rats dosed with 2000 mg/kg died. 2/5 male and 3/5 female rats dosed with 1000 mg/kg died. Rats in the 2 highest dose groups were lethargic after dosing. Other toxic responses in these 2 dose groups included blood around the mouth and nose, subcutaneous hemorrhages, and blood in the urinary and gastrointestinal tract. Animals administered lower doses had no compound-related histologic lesions.  
**Source:** Bayer AG Leverkusen

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## 5. Toxicity

date: 18-FEB-2000  
Substance ID: 100-51-6

**Species:** rat **Sex:** male/female  
**Strain:** other: F344/N  
**Route of admin.:** gavage  
**Exposure period:** 13 w  
**Frequency of treatment:** daily  
**Post. obs. period:** no  
**Doses:** 50, 100, 200, 400, 800 mg/kg/d  
**Control Group:** yes  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** No. of animals: 10/sex/dose.  
**Result:** 8/10 male rats dosed with 800 mg/kg died during w 7 and 8. Rats of the high dose group exhibited clinical signs indicative of neurotoxicity including staggering, respiratory difficulty, and lethargy. Hemorrhages occurred around the mouth and nose, and there were histologic lesions in the brain, thymus, skeletal muscle, and kidney. There were reductions in relative weight gain in male rats dosed with 800 mg/kg and in female rats dosed with 200 mg/kg or more. No notable changes in bw gain or compound-related histopathologic lesions were observed in rats from the lower dose groups.  
**Source:** Bayer AG Leverkusen

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**Species:** rat **Sex:** male/female  
**Strain:** no data  
**Route of admin.:** gavage  
**Exposure period:** 3 w  
**Frequency of treatment:** 6 d/w  
**Post. obs. period:** no  
**Doses:** 50, 150, 500 mg/kg  
**Control Group:** yes  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** No. of animals: 5/sex/dose.  
**Result:** The compound was administered in propylene glycol. Increases in weight were the same in all groups, and there were no pathological effects on blood or organs.  
**Source:** Bayer AG Leverkusen

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## 5. Toxicity

date: 18-FEB-2000  
Substance ID: 100-51-6

**Species:** mouse **Sex:** no data  
**Strain:** no data  
**Route of admin.:** gavage  
**Exposure period:** 8 d  
**Frequency of treatment:** daily  
**Post. obs. period:** no data specified  
**Doses:** 325, 645, 1300, 2595 mg/kg/d  
**Control Group:** no data specified  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** No. of animals: no data.  
**Result:** Muscle incoordination, a "hunched" appearance, depression, and fur changes were reported in mice given 645 mg/kg but not in those receiving 325 mg/kg or below. At 1300 mg/kg, animals additionally suffered breathing difficulties, discharge from the eyes, and various CNS effects, and death occurred on the 1. d in all mice given 2595 mg/kg.  
**Source:** Bayer AG Leverkusen

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**Species:** mouse **Sex:** male/female  
**Strain:** B6C3F1  
**Route of admin.:** gavage  
**Exposure period:** 16 d  
**Frequency of treatment:** daily  
**Post. obs. period:** no data specified  
**Doses:** 125, 250, 500, 1000, 2000 mg/kg/d  
**Control Group:** no data specified  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** No. of animals: 5/sex/dose.  
**Result:** All male and female mice dosed with 2000 mg/kg died. 1/5 male and 2/5 female mice dosed with 1000 mg/kg died. Mice of each sex in the 2 highest dose groups were lethargic after dosing. Other toxic responses in these 2 dose groups included blood around the mouth and nose, subcutaneous hemorrhages, and blood in the urinary and gastrointestinal tract and in the urinary bladder. Animals administered lower doses had no compound-related histologic lesions.  
**Source:** Bayer AG Leverkusen

(40)

**Species:** mouse **Sex:** male/female  
**Strain:** B6C3F1  
**Route of admin.:** gavage  
**Exposure period:** 13 w  
**Frequency of treatment:** daily  
**Post. obs. period:** no  
**Doses:** 50, 100, 200, 400, 800 mg/kg/d  
**Control Group:** yes  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** No. of animals: 10/sex/dose.  
**Result:** Staggering after dosing occurred during the first 2 w of the study in mice dosed with 800 mg/kg. There were reductions in relative weight gain in male mice dosed with 400 or 800 mg/kg, and in female mice dosed with 200 mg/kg or more. No notable changes in bw gain or compound-related histopathologic lesions were observed in mice from the lower dose groups.  
**Source:** Bayer AG Leverkusen

(40)

### 5.5 Genetic Toxicity 'in Vitro'

**Type:** Ames test  
**System of testing:** S. typhimurium TA 98, TA 100, TA 1535, TA 1537  
**Concentration:**  
**Metabolic activation:** with and without  
**Result:** negative  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen

(93)

**Type:** Ames test  
**System of testing:** S. typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538  
**Concentration:**  
**Metabolic activation:** without  
**Result:** negative  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen

(94)

Type: Ames test  
System of testing: S. typhimurium TA 98, TA 100, TA 1535, TA 1537  
Concentration:  
Metabolic activation: with and without  
Result: negative  
Method:  
Year: GLP:  
Test substance:  
Remark: Rat and hamster liver S-9 mix.  
Source: Bayer AG Leverkusen

(95) (96)

Type: Ames test  
System of testing: S. typhimurium TA 98, TA 100  
Concentration:  
Metabolic activation: without  
Result: negative  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen

(97)

Type: Ames test  
System of testing: S. typhimurium TA 92, TA 94, TA 98, TA 100, TA 1535, TA 1537  
Concentration:  
Metabolic activation: with  
Result: negative  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen

(98)

Type: Ames test  
System of testing: S. typhimurium TA 98, TA 1535  
Concentration:  
Metabolic activation: no data  
Result: negative  
Method:  
Year: GLP:  
Test substance:  
Source: Bayer AG Leverkusen

(99)

**Type:** Ames test  
**System of testing:** S. typhimurium TA 100  
**Concentration:**  
**Metabolic activation:** without  
**Result:** negative  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (100)

**Type:** Bacillus subtilis recombination assay  
**System of testing:** B. subtilis M 45, H 17  
**Concentration:**  
**Metabolic activation:**  
**Result:** positive  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (101)

**Type:** Bacillus subtilis recombination assay  
**System of testing:** B. subtilis M 45, H 17  
**Concentration:**  
**Metabolic activation:**  
**Result:** positive  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (102)

**Type:** Cytogenetic assay  
**System of testing:** CHO cells  
**Concentration:** up to 5000 ug/ml DMSO  
**Metabolic activation:** without  
**Result:** negative  
**Method:** other: Galloway S.M. et al., Environ. Mutagen. 7, 1-52 (1985)  
**Year:** 1989 **GLP:** no data  
**Test substance:** other TS  
**Source:** Bayer AG Leverkusen (103) (40) (96)

**Type:** Cytogenetic assay  
**System of testing:** CHO cells  
**Concentration:** up to 5000 ug/ml DMSO  
**Metabolic activation:** with  
**Result:** positive  
**Method:** other: according to Galloway S.M. et al. Environm. Mutagen.7, 1-52 (1985)  
**Year:** 1989 **GLP:** no data  
**Test substance:** no data  
**Source:** Bayer AG Leverkusen

(103) (40) (96)

**Type:** Cytogenetic assay  
**System of testing:** CHL cells  
**Concentration:**  
**Metabolic activation:**  
**Result:** negative  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen

(98) (104)

**Type:** Mouse lymphoma assay  
**System of testing:** L5178Y cells  
**Concentration:** up to 5000 ug/ml DMSO  
**Metabolic activation:** without  
**Result:** negative  
**Method:** other: according to Myhr B. et al., Prog. Mutat. Res. 5, 555-568 (1985)  
**Year:** 1989 **GLP:** no data  
**Test substance:** no data  
**Remark:** The effect was associated with toxicity.  
**Source:** Bayer AG Leverkusen

(40)

**Type:** Mouse lymphoma assay  
**System of testing:** L5178Y cells  
**Concentration:** up to 5000 ug/ml DMSO  
**Metabolic activation:** with  
**Result:** positive  
**Method:** other: according to Myhr G. et al., Prog. Mutat. Res. 5, 555-586 (1985)  
**Year:** 1989 **GLP:** no data  
**Test substance:** no data  
**Source:** Bayer AG Leverkusen

(40)

**Type:** Mouse lymphoma assay  
**System of testing:** L5178Y tk+/tk- cells  
**Concentration:**  
**Metabolic activation:** with and without  
**Result:** ambiguous  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (105) (106) (96)

**Type:** Sister chromatid exchange assay  
**System of testing:** CHO cells  
**Concentration:** up to 5000 ug/ml DMSO  
**Metabolic activation:** with and without  
**Result:** ambiguous  
**Method:** other: according to Galloway S.M. et al., Environ. Mutagen. 7, 1-52 (1985)  
**Year:** 1989 **GLP:** no data  
**Test substance:** other TS  
**Source:** Bayer AG Leverkusen (103) (40)

**Type:** Sister chromatid exchange assay  
**System of testing:** CHO cells  
**Concentration:**  
**Metabolic activation:** with and without  
**Result:** positive  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (96)

**Type:** other: DNA Double Strand Breaks  
**System of testing:** rat hepatocytes  
**Concentration:** 0, 1, 3, 10 mM in 1 % DMSO  
**Metabolic activation:** no data  
**Result:** ambiguous  
**Method:** other: in vitro alkaline elution assay  
**Year:** 1994 **GLP:** no data  
**Test substance:** no data  
**Remark:** positive only in the highest dose  
**Source:** Bayer AG Leverkusen (107) (108)

**Type:** other: Point-mutation  
**System of testing:** E. coli  
**Concentration:**  
**Metabolic activation:** with and without  
**Result:** negative  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (109) (110)

**Type:** other: Point-mutation  
**System of testing:** E. coli WP2 uvrA  
**Concentration:**  
**Metabolic activation:** no data  
**Result:** negative  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (101)

**Type:** other: Point-mutation  
**System of testing:** E. coli WP2 uvrA  
**Concentration:**  
**Metabolic activation:** without  
**Result:** negative  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Bayer AG Leverkusen (102)

**Type:** other: transformation assay  
**System of testing:** BALB/c-3T3 cells  
**Concentration:** no data  
**Metabolic activation:** no data  
**Result:** positive  
**Method:** other: Matthews E.J., J. Tissue Culture Methods 10, 157-164 (1986), Matthewy E.J. et al., Environm. Health Perspect. 101 [Suppl 2], 319-345 (1993)  
**Year:** 1993 **GLP:** no data  
**Test substance:** no data  
**Source:** Bayer AG Leverkusen (111)

**5.6 Genetic Toxicity 'in Vivo'**

**Type:** Drosophila SLRL test  
**Species:** Drosophila melanogaster **Sex:** male  
**Strain:** other: Canton S  
**Route of admin.:** drinking water  
**Exposure period:** 72 hrs  
**Doses:** 0, 5000 (unit not given) in 5 % succrose solution  
**Result:**  
**Method:** other  
**Year:** 1994 **GLP:** no data  
**Test substance:** other TS: purity: 99.8 %  
**Result:** no evidence for mutagenicity  
**Source:** Bayer AG Leverkusen

(112)

**Type:** Drosophila SLRL test  
**Species:** Drosophila melanogaster **Sex:** male  
**Strain:** other: Canton S  
**Route of admin.:** i.p.  
**Exposure period:** once  
**Doses:** 0, 8000 (unit not given)  
**Result:**  
**Method:** other  
**Year:** 1994 **GLP:** no data  
**Test substance:** other TS: purity.99.8 %  
**Result:** no evidence for mutagenicity  
**Source:** Bayer AG Leverkusen

(112)

**Type:** Micronucleus assay  
**Species:** mouse **Sex:** male  
**Strain:**  
**Route of admin.:** i.p.  
**Exposure period:** 24 h  
**Doses:** 50, 100, 200 mg/kg  
**Result:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** No. of animals: 6/dose.  
**Result:** There was no indication of micronucleus induction at any dose tested.  
**Source:** Bayer AG Leverkusen

(113)

**Type:** other: replicative DNA synthesis  
**Species:** rat **Sex:** male  
**Strain:** Fischer 344  
**Route of admin.:** gavage  
**Exposure period:** once  
**Doses:** 0, 300, 600 mg/kg bw  
**Result:**  
**Method:** other: according to Uno Y. et al., Toxicol. Lett. 63, 191-199, 201-209 (1992)  
**Year:** 1994 **GLP:** no data  
**Test substance:** no data  
**Result:** Benzylalkohol did not induce replicative DNA synthesis in rat hepatocytes following oral treatment.  
**Source:** Bayer AG Leverkusen

(114)

**Type:** other: replicative DNA synthesis  
**Species:** mouse **Sex:** male  
**Strain:** B6C3F1  
**Route of admin.:** gavage  
**Exposure period:** once  
**Doses:** 0, 400, 800 mg/kg bw  
**Result:**  
**Method:** other: according to Uno Y. et al., Toxicol. Lett. 63, 191-199, 201-209 (1992),  
**Year:** 1995 **GLP:** no data  
**Test substance:** no data  
**Result:** Benzylalkohol did not induce replicative DNA synthesis in mice hepatocytes following oral treatment.  
**Source:** Bayer AG Leverkusen

(115)

### 5.7 Carcinogenicity

**Species:** rat **Sex:** male/female  
**Strain:** other: F344/N  
**Route of admin.:** gavage  
**Exposure period:** 103 w  
**Frequency of treatment:** 5 d/w  
**Post. obs. period:** no  
**Doses:** 200, 400 mg/kg/d  
**Result:**  
**Control Group:** yes  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** No. of animals: 50/sex/dose.  
**Result:** Benzyl alcohol was administered in corn oil. No effect on bw gain or mortality was observed. No apparent compound-related nonneoplastic responses were observed. There was no evidence of carcinogenic activity.  
**Source:** Bayer AG Leverkusen

(116) (40)

**Species:** mouse **Sex:** male/female  
**Strain:** B6C3F1  
**Route of admin.:** gavage  
**Exposure period:** 103 w  
**Frequency of treatment:** 5 d/w  
**Post. obs. period:** no  
**Doses:** 100, 200 mg/kg/d  
**Result:**  
**Control Group:** yes  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** No. of animals: 50/sex/dose.  
**Result:** Benzyl alcohol was administered in corn oil. No effects on bw gain or mortality was observed. No apparent compound-related nonneoplastic responses were observed. There was no evidence of carcinogenic activity.  
**Source:** Bayer AG Leverkusen

(116) (40)

**Species:** mouse **Sex:** male  
**Strain:** B6C3F1  
**Route of admin.:** i.p.  
**Exposure period:** 22 d  
**Frequency of treatment:** once on day 1, 8, 15, 22  
**Post. obs. period:** up to 1 a  
**Doses:** 3.75 umol (total dose) in trioctanoin  
**Result:**  
**Control Group:** yes  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** 35 mice received injections prior to weaning. The mice were weaned at 4 weeks of age. All surviving mice were killed at 12 months for enumeration of hepatomas.  
**Result:** Benzyl alcohol had no detectable activity for the initiation of hepatic tumors on administration to male mice prior to weaning.  
**Source:** Bayer AG Leverkusen

(117)

### 5.8 Toxicity to Reproduction

-

**5.9 Developmental Toxicity/Teratogenicity**

**Species:** mouse **Sex:** female  
**Strain:** CD-1  
**Route of admin.:** gavage  
**Exposure period:** 8 d (d 6-13 of gestation)  
**Frequency of treatment:** daily  
**Duration of test:**  
**Doses:** 750 mg/kg bw/d  
**Control Group:** yes  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** No. of animals: no data.  
Post observation: until 3 d after pregnancy  
**Result:** Reduced birth weight and decreased growth were seen in the  
pups. The dams showed increased mortality.  
**Source:** Bayer AG Leverkusen (118) (119)

**Species:** other: chicken embryo **Sex:**  
**Strain:**  
**Route of admin.:** other  
**Exposure period:** 11 to 18 d  
**Frequency of treatment:** 1 injection before incubation or on different d after  
incubation  
**Duration of test:**  
**Doses:** 0.01-0.02 ml/egg = 10-20 mg/egg  
**Control Group:** yes  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Injections of benzyl alcohol into the yolks of fertile  
eggs, either before incubation, or from the 1. through the  
7. d after the beginning of their incubation give rise to  
meningoceles, limb deformities, beak defects such as, arched  
upper beaks, localized blebs and generalized edema.  
no post observation  
**Source:** Bayer AG Leverkusen (120)

**Species:** mouse **Sex:**  
**Strain:**  
**Route of admin.:**  
**Exposure period:**  
**Frequency of treatment:**  
**Duration of test:**  
**Doses:**  
**Control Group:**  
**Method:** other: according to Chernoff and Kavlock: short time in vivo assay (no further information)  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Remark:** abstract only  
**Result:** According to the method used an intermediate priority classification was derived.  
**Source:** Bayer AG Leverkusen

(121)

### 5.10 Other Relevant Information

**Type:** Metabolism  
**Remark:** Humans, rabbits and rats readily oxidize benzyl alcohol to benzoic acid, which, after conjugation with glycine, is rapidly eliminated as hippuric acid in the urine.  
**Source:** Bayer AG Leverkusen  
 (122) (123) (124) (125) (126) (127) (128)

**Type:** other  
**Remark:** Bacillus subtilis spore rec-assay can be used as a simple screening test taking the place of animal methods for detection of the allergenicity.  
**Source:** Bayer AG Leverkusen  
 (129)

**Type:** other  
**Remark:** yeast test: according to the author an alternative to the contemporary mode of acute toxicity testing. In the test, the increase in the cell count after treatment in relationship to the increase in cell count of untreated cells is measured and expressed as "medium inhibitory concentration = IC 50 " : benzyl alcohol IC 50 = 277 mg/l  
**Source:** Bayer AG Leverkusen  
 (130) (131)

**Type:** other  
**Remark:** Benzylalkohol differentially altered the specific activity of subcellular rat epididymal and testicular aldehyde dehydrogenase activity as well as hepatic aldehyde dehydrogenase activity.  
**Source:** Bayer AG Leverkusen  
 (132) (133) (134) (135)

- Type:** other  
**Remark:** different concentrations of benzyl alcohol (1,2,5,10 % v/v) in sesame oil were subcutaneously injected to rats. only the 1 % benzyl alcohol produced an insignificant increase in skin fold thickness.  
**Source:** Bayer AG Leverkusen (136)
- Type:** other  
**Remark:** In vitro, benzyl alcohol relaxes airway smooth muscle, probably through the decrease in intracellular Ca<sup>2+</sup> release by inhibiting agonist-mediated phosphatidylinositol turnover.  
**Source:** Bayer AG Leverkusen (137)
- Type:**  
**Remark:** Aseptic meningitis has been observed following intrathecal administration of radiopharmaceuticals that contain benzylalcohol as a preservative. Cisterna magna injections of benzylalcohol in concentrations as high as 10 times that normally used did not produce meningitis in adult or immature dogs. With 9 % benzyl alcohol, transient respiratory arrest was observed in adult dogs and death was observed in immature dogs; 7 % and 4.5 % benzyl alcohol produced clonic seizures in puppies.  
**Source:** Bayer AG Leverkusen (138)
- Type:**  
**Remark:** Injection of benzyl alcohol (700-900 mg/kg, i.p.) caused rapid immobilization of mice. The mice were immobilized within 2 min. and remained unresponsive (no righting reflex, no wink reflex, and no leg reflex) for about 30 min. The immobilizing effect was accompanied by a marked hyperglycemia. Tracer studies indicated that the hyperglycemic effect may have resulted from increased gluconeogenesis.  
**Source:** Bayer AG Leverkusen (139)
- Type:**  
**Remark:** Benzyl alcohol used as a stabilizer for antibiotics of aminoglycosid structure is the substance responsible for the displacement of bilirubin from albumin. The free, unbound, unconjugated bilirubin tends to diffuse into the lipid of the brain of young Gunn rats with resultant kernicterus.  
**Source:** Bayer AG Leverkusen (140)

**Type:****Remark:**

Duodenal and jejunal brush border membrane vesicle integrity was studied after in vitro treatment of rabbit tissue with benzylalcohol. The effect of the alcohol on gastric parietal cell apical and microsomal membrane vesicle integrity was also studied. Exposure of vesicles to the alcohol caused concentration dependent decreases in enclosed volume. All concentrations tested reduced the enclosed volume of both gastric apical membrane vesicles and gastric microsomes. The alcohol induced disruption of the vesicle membranes appears to result from a fluidising effect. The main effect of the raised fluidity is to increase membrane fragility.

**Source:**

Bayer AG Leverkusen

(141) (142)

**Type:****Remark:**

Benzyl alcohol as a fragrance ingredient used in cosmetic and other products is lipophilic and therefore has the potential to be readily absorbed through skin. The percutaneous absorption was determined in vivo in rhesus monkeys. Absorption through occluded skin was high (56-80 %) in 24 h. No correlation was seen between skin penetration and the octanol-water partition coefficient. Under unoccluded conditions skin penetration was reduced (32 %), because of evaporation of the compound.

**Source:**

Bayer AG Leverkusen

(143)

**Type:****Remark:**

After i.v. injection in mice, benzyl alcohol was found to inhibit TBPS binding and to stimulate GABA receptor mediated Cl influx into brain vesicles.

**Source:**

Bayer AG Leverkusen

(144)

**Type:****Remark:**

Benzyl alcohol can cause hemolysis of human and rabbit erythrocytes in the presence of 0.9 % NaCl.

**Source:**

Bayer AG Leverkusen

(145) (146)

**Type:****Remark:**

Benzyl alcohol produced up to 6-fold increases in cAMP concentrations in purified human peripheral blood lymphocytes. Significant but less marked augmentation of cAMP was observed in human platelets, human granulocytes, and rabbit alveolar macrophages. The mechanism of the alcohol-induced cAMP accumulation is probably secondary to membrane perturbation and consequent activation of adenylate cyclase.

**Source:**

Bayer AG Leverkusen

(147)

- Type:**  
**Remark:** Uncoupled sonic submitochondrial particles from beef heart and rat liver were studied for mitochondrial electron transport. Benzyl alcohol was found to inhibit each of the segments of the electron transport chain assayed. NADH oxidase and NADH-cytochrome c oxido-reductase required the lowest concentration for inhibition, and cytochrome c oxidase required the highest concentration. Beef heart submitochondrial particles are less sensitive to inhibition than are rat liver particles.
- Source:** Bayer AG Leverkusen (148)
- Type:**  
**Remark:** Lactated Ringer's solution containing 1.5 % benzyl alcohol can cause severe symptoms of toxicity in cats including hyperesthesia leading to depression, coma, and finally death. In the cat, only hippuric acid is formed, as this species lacks adequate glucuronic acid conjugation capacity, resulting in a decreased rate of metabolism. This results in an accumulation of benzoic acid. Benzoic acid has been shown to be extremely toxic to cats, causing clinical signs similar to those observed.
- Source:** Bayer AG Leverkusen (149)
- Type:**  
**Remark:** 50 mM benzyl alcohol fluidized proximal brush-border membranes prepared from human small intestine and increased p-nitrophenyl-phosphatase activity in this membrane. This agent also shifted the phase transition temperature of the membrane and breakpoint temperature of this enzymatic activity.
- Source:** Bayer AG Leverkusen (150)
- Type:**  
**Remark:** Microscopic examination revealed local nerve degeneration when 5 % benzyl alcohol was injected into the side of a cat's face. At 10 % local anaesthesia was produced.
- Source:** Bayer AG Leverkusen (151)
- Type:**  
**Remark:** Benzyl alcohol displays a pronounced antiarrhythmic-anti-fibrillatory effect, when injected i.v. into dogs and rats with spontaneous or drug-induced arrhythmias. Mechanisms which might be responsible for the antiarrhythmic effect: lengthening of the effective refractory period, local and general anaesthetic effects, changes of osmolality. The i.v. injection of benzyl- alcohol in high doses, produces intravascular haemolysis.
- Source:** Bayer AG Leverkusen (152)

- Type:**  
**Remark:** The length of the oestrus cycle was reduced when 0.52-2.1 d (1-4 mg/kg bw) benzyl alcohol was injected into the uterus of each of 48 cows.  
**Source:** Bayer AG Leverkusen (153)
- Type:**  
**Remark:** The in vitro effect of local anesthetic benzyl alcohol was studied using isolated cells from rat stomach. Lower concentrations of the alcohol increased the basal aminopyrine accumulation and potentiated the secretory response of parietal cells to histamine and dbcAMP. At higher concentrations the alcohol progressively inhibited both the basal 14-C-aminopyrine accumulation and that stimulated by histamine, dbcAMP or carbachol. While a low concentration increased gastric microsomal (H-K)-ATPase activity, higher concentrations inhibited enzyme activity to about 80 % of those activities found in resting parietal cells.  
**Source:** Bayer AG Leverkusen (154)
- Type:**  
**Remark:** Benzyl alcohol is a fairly efficient anesthetic for intact mucous membranes, greatly surpassing procain. Its action is not as lasting as that of cocain. It appears that 1 % does not produce satisfactory anesthesia of the tongue, even after 10 min. contact.  
**Source:** Bayer AG Leverkusen (155)
- Type:**  
**Remark:** Benzyl alcohol in non-toxic concentrations was found to markedly reduce the hemoglobin minor/hemoglobin major ratio and to moderately reduce the total hemoglobin induced by DMSO or HMBA in mouse erythro leukemia (MEL) cells, while only slightly decreasing the ratio induced by hemin or butyrate.  
**Source:** Bayer AG Leverkusen (156)
- Type:**  
**Remark:** It was demonstrated that benzyl alcohol, a neutral local anesthetic, inhibits the uptake and degradation of lowdensity lipoprotein and endocytosis of transferrin receptors of guinea-pig leukemic B lymphocytes. This inhibition is very rapid, concentration dependant and reversible by simple washing. Membrane fluidity of the living cells is also modified.  
**Source:** Bayer AG Leverkusen (157)

**Type:**  
**Remark:** The tissue culture lethal dose (TCLD50) in mouse embryo cells was found to be 0.002 mg/ml.  
**Source:** Bayer AG Leverkusen (158)

**Type:**  
**Remark:** Benzyl alcohol is more toxic to infant jaundiced (jj) than to non-jaundiced (Jj) Gunn rats. Before excretion as hippuric acid, benzyl alcohol is metabolized to benzoic acid, a potent competitor for bilirubin-albumin binding sites. These pathways are immature in newborns. Therefore the kernicterus in jj pups is probably due to increased levels of unbound bilirubin.  
**Source:** Bayer AG Leverkusen (159)

**Type:**  
**Remark:** The plasma half-life of benzyl alcohol administered as a 2.5 % solution in saline was found to be approximately 1.5 h in dogs injected i.v. at doses of 52 and 105 mg/kg.  
**Source:** Bayer AG Leverkusen (41)

**Type:**  
**Remark:** Larger percentages of benzyl alcohol doses were found in urine as benzoic acid in preterm babies, while less hippuric acid appeared in their urine than in term newborns. These results indicate that hippuric acid formation is deficient in preterm neonates.  
**Source:** Bayer AG Leverkusen (160)

**Type:**  
**Remark:** In vitro studies of human liver alcohol dehydrogenase (ADH) variants revealed that benzyl alcohol is slowly metabolized by beta-2-ADH. Working with this solvent might lead to toxic effects; these could be particularly prominent in individuals possessing the beta-2-ADH if they have a lower capacity to eliminate them, or they could be particularly prominent in those with beta-1-ADH if they quickly convert them into toxic aldehydes.  
**Source:** Bayer AG Leverkusen (161)

**Type:**  
**Remark:** Perfusing the anterior chamber of enucleated rabbit eyes with 1.18 % benzyl alcohol, the corneal endothelial cells changed the appearance and the corneas began to swell.  
**Source:** Bayer AG Leverkusen (162)

**Type:**

**Remark:** The invitro effects of benzyl alcohol and benzaldehyde on subcellular rat liver NAD-dependant alcohol and aldehyde dehydrogenase were studied as a function of gender. These effects were compared with those of the primary substrates ethanol and acetaldehyde. the results suggest metabolic competitions between benzyl alcohol and ethyl alcohol for catalysis by alcohol dehydrogenase.

**Source:** Bayer AG Leverkusen

(163)

**Type:**

**Remark:** Acute intravenous toxicity of benzyl alcohol was determined in CD2F1 (0.05-0.2 ml/kg bw), B6D2F1 (0.05-0.4 ml/kg) and C57BL/6 mice. The lowest dose was a safe dose and the highest one was the dose causing mortality in no more than half the animals of each group. Clinical signs were convulsion, dyspnea and reduced mortality in all strains for 24 hours. The slight decrease in body weight in the first week following treatment returned to normal in the second week.

**Source:** Bayer AG Leverkusen

(164)

**5.11 Experience with Human Exposure**

**Remark:** Benzyl alcohol poisoning can cause the gasping syndrome in neonates. The infants had a typical course of gradual neurologic deterioration, severe metabolic acidosis, the striking onset of gasping respirations, thrombocytopenia, hepatic and renal failure, hypotension, cardiovascular collapse and death. In every infant, unmetabolized benzyl alcohol was identified in the urine.

**Source:** Bayer AG Leverkusen

(165) (166) (167) (168) (169) (170) (171) (172)

**Remark:** Local anaesthesia occurred when neat benzyl alcohol was applied to the (presumably uncovered) skin or when 1 % aqueous solution was injected intradermally.

**Source:** Bayer AG Leverkusen

(34)

**Remark:** A methylprednisolone sodium succinate formulation, containing 18 mg / dose of benzyl alcohol, was well tolerated in human volunteers after i.v. injection. No important drug-related side effects were encountered.

**Source:** Bayer AG Leverkusen

(173)

**Remark:** Cases of allergic contact dermatitis, and even systemic hypersensitivity have been reported in humans.

**Source:** Bayer AG Leverkusen

(174) (175) (176) (177) (178) (179) (180) (181) (182) (183) (184)  
(185)

- Remark:** No contact allergy could be detected in humans treated with a 10 % formulation of benzyl alcohol (no other data).  
**Source:** Bayer AG Leverkusen (186)
- Remark:** Premature neonates may receive multiple drugs in the neonatal intensive care unit, some of which may contain benzyl alcohol. As there may be no safe lower dose of benzyl alcohol in these patients, it would seem prudent to avoid the use of multiple dose vials containing benzyl alcohol whenever alternatives exist.  
**Source:** Bayer AG Leverkusen (187)
- Remark:** It also seems prudent to avoid the use of products containing benzyl alcohol to pregnant patients within whom the benzyl alcohol molecule, given its small size, presumably crosses the placental barrier into immature fetal tissues as readily as it crosses the blood-brain barrier.  
**Source:** Bayer AG Leverkusen (188)
- Remark:** high levels of benzyl alcohol (5-500 ug/10 ml plasma) were found in uremic patients on hemodialysis; benzyl alcohol was not detected in normal controls.  
**Source:** Bayer AG Leverkusen (189)
- Remark:** In 2 long-term double blind studies on humans comparing benzyl alcohol, placebo and Catalin in the topical treatment of progressive cataract, rapid (2-3 weeks treatment) reversal of incipient cataract was obtained accompanied by a marked improvement of vision and by a significantly lower percentage of eyes requiring surgery after 22 months of treatment with benzyl alcohol than with placebo and Catalin.  
**Source:** Bayer AG Leverkusen (190)
- Remark:** Study on healthy adult volunteers: Benzyl alcohol is itself an effective anesthetic and can reduce the pain of injection for lidocaine without adversely affecting its anesthetic properties.  
**Source:** Bayer AG Leverkusen (191)
- Remark:** Benzyl alcohol is commonly used as a preservative in many injectable drugs and solutions. A number of neonatal deaths and severe respiratory and metabolic complications in low-birth-weight premature infants have been associated with the use of this agent.  
**Source:** Bayer AG Leverkusen (192) (193) (194) (195) (196) (197) (198)

- (1) Chemiekaarten, negende editie, 1993-1994  
Uitgave van:
  - NIA
  - VNCI
  - samson H.D. Tjeen Willink
- (2) Bayer AG, Sicherheitsdatenblatt Benzylalkohol, 20.06.1989
- (3) Auer-Technikum, Auerges. mbH Berlin, 12. Ausg. 1988
- (4) Calculation UWS-Produktsicherheit, Bayer AG 1991
- (5) THOR database Pomona 89, MedChem Software 1989. Daylight, Chemical Information Systems, Claremont, CA 91711, USA
- (6) Safety Data Sheet Bayer AG 12.10.1992
- (7) Bayer AG data
- (8) Meinck, F. et al., Industrie-Abwaesser, p. 41 (1968)
- (9) Gerike, P. and Gode, P., Chemosphere 21(6), 799-812 (1990)
- (10) Wagner, R., Vom Wasser 47, 241-265 (1976)
- (11) Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan, Compiled under the Supervision of Chemical Products Safety Division, Basic Industries Bureau MITI, Ed. by CITI, October 1992. Published by Japan Chemical Industry Ecology-Toxicology & Information Center
- (12) Wagner, R., Vom Wasser 42, 271-305 (1974)
- (13) Horowitz, A. et al., Dev. Ind. Microbiol. 23, 435-444 (1982)
- (14) Urano, K. und Kato, Z., Journal of Hazardous Materials 13 (2), 135-145 (1986)
- (15) NAPM (National Association of Photographic Manufacturers, Inc., in cooperation with Hydroscience, Inc.): Environmental Effect of Photoprocessing Chemicals, Vol I and II. NAPM, Inc., 600 Mamaroneck Ave., Harrison, N.Y., 10528 (1974)
- (16) Knie, J. et al., Deutsche Gewaesserkundl. Mitt. 27 (3), 77-79 (1983)
- (17) Applegate, V.C. et al., Special Scientific Report-Fisheries No. 207, Washington, D.C., March 1957
- (18) Lipnick, R.L. et al., Environmental Toxicology and Chemistry 4, 281-296, (1985)

- (19) Loeb, H.A. und Kelly, W.H., Special Scientific Report-Fisheries No. 471, Washington, D.C. (1963)
- (20) Dawson, G.W. et al., Journal of Hazardous Materials 1, 303-318 (1975/77)
- (21) Mattson, V.R. et al., EPA-600/3-76-097, Oct. 1976, PB-262 897
- (22) Bringmann, G. und Kuehn, R., Gesundheitsingenieur 80 (4), 115-120 (1959)
- (23) Bringmann, G. und Kuehn, R., Z. Wasser Abwasser Forsch. 15 (1), 1-6 (1982)
- (24) Stratton, G.W. und Corke, C.T., Environmental Pollution (Series A) 29 (1), 71-80 (1982)
- (25) Kaiser, K.L.E. et al., QSAR of acute toxicity of mono-substituted benzene derivatives to photobacterium phosphoreum. QSAR Environ. Toxicol., Proc. Int. Workshop, 2nd Meeting Date 1986, Edited by Kaiser, K.L.E., Reidel: Dordrecht, Neth., 153-168 (1987)
- (26) Ferard, J.F. et al., Sciences de l'eau 2 (2), 221-237 (1983)
- (27) Blum, D.J.W. und Speece, R.E, Research Journal WPCF 63(3), 198-207 (1991)
- (28) Sinniah, B., Transactions of the Royal Society of Tropical Medicine and Hygiene 77 (1), 35-38 (1983)
- (29) Loeser, E.: Bayer AG data, short report, 3. 11. 1978
- (30) Jenner, P. M. et al.: Fd. Cosmet. Toxicol. 2, 327-343 (1964)
- (31) Graham, B. E., Kuizenga, M. H.: J. Pharmac. 84, 358-362 (1945)
- (32) Opdyke, D. L. J.: Fd. Cosmet. Toxicol. 11, 1011-1013 (1973)
- (33) Smyth, H. F. et al.: Arch. Ind. Hyg. Occup. Med. 4, 119-120 (1951)
- (34) Macht, D. I.: J. Pharmac. exp. Ther. 11, 263-279 (1918)
- (35) Carter, D. V. et al.: J. Pharmacol., Suppl. 10, T149-T159 (1958)
- (36) Bayer AG data, Report No. 19799, 12. 12. 1990
- (37) Patty's Industrial Hygiene and Toxicology, Third Revised Edition, Vol. 2C, pg. 4639 (1982), John Wiley and Sons

- (38) NPIRI: Raw Mater. Data Handb. Vol. 1, 6 (1974)
- (39) McCloskey, S.E. et al., J. Pharmaceut. Sciences 75, 702-705 (1986)
- (40) NTP: Technical Report No. TR 343 (1989)
- (41) Kimura, E. T. et al.: Toxicol. Appl. Pharmacol. 18, 60-68 (1971)
- (42) Chvapil, M. et al.: Arch. int. Pharmacodyn. 85, 330-343 (1962)
- (43) Bayer AG data, Report No. 19232, 6. 7. 1990
- (44) Cebula, T. A. et al.: Infection and Immunity 44, 91-96 (1984)
- (45) Motoyoshi, K. et al.: Cosmet. Toiletries 94, 41-48 (1979)
- (46) Thyssen, J.: Bayer AG data, short report, 2. 1. 1979
- (47) Klecak, G. et al.: J. Soc. Cosmet. Chem. 28, 53-64 (1977)
- (48) Sharp, D. W.: Toxicology 9, 261-271 (1978)
- (49) Takenaka, T. et al.: Parf. Cosm. Sav. 13, 699-706 (1970)
- (50) Emmons, W. W., Marks, J. G.: Contact Dermatitis 13, 258-265 (1985)
- (51) Lashmar, U. T. et al.: J. Pharm. Pharmacol. 41, 118-121 (1989)
- (52) Macht, D. I., Shohl, A. T.: J. Pharmac. exp. Ther. 16, 61-69 (1921)
- (53) Hayakawa, R. et al.: Skin Res. 30, 243-246 (1988)
- (54) Mitchell, D. M., Beck, M. H.: Contact Dermatitis 18, 301-302 (1988)
- (55) Malten, K. E. et al.: Contact Dermatitis 11, 1-10 (1984)
- (56) Mitchell, J. C. et al.: Contact Dermatitis 8, 336-337 (1982)
- (57) Nethercott, J. R.: Contact Dermatitis 8, 389-395 (1982)
- (58) Fisher (1975) cited in: Etain Cronin, Contact Dermatits, Churchill Livingstone, Edinburgh, London, New York, 1980, p. 807

- (59) Schultheiss (1957) cited in: Etain Cronin, Contact Dermatitis, Churchill Livingstone, Edinburgh, London, New York, 1980, p. 807
- (60) Kashima R. et al., Contact dermatitis 28, 235-242 (1993)
- (61) Kashima R. et al., Contact dermatitis 29, 26-32 (1993)
- (62) Maurer Th. Durr. Probl. Derm. 14, 114-151 (1985)
- (63) Sharp D.W., Toxicology 9, 261-271 (1978)
- (64) Adams R. M. in Maibach H.I., G.A. Gellin (eds.), Occupational and Industrial Dermatology, Chicago, Year Book Publishers, Inc., p. 345-352 (1982)
- (65) Aguirre A. et al., Contact Dermatitis 30, 52-53 (1994)
- (66) Angenelli G. et al., J. Appl. Cosmetol. 3, 223-236 (1985)
- (67) Arima Y. et al., Skin Res. 31 [Suppl. 7], 221-225 (1989)
- (68) Brasch J. et al., Dermatosen 41, 71-76 (1993)
- (69) Commandeur C. et al., Allergy 47, 337-339 (1992)
- (70) Conde-Salazar L. et al., Actas Dermo-Sif. 83, 383-386 (1992)
- (71) Corazza M. et al., Contact Dermatitis 34, 74-75 (1996)
- (72) Edwards E.K., Cutis 28, 332-333 (1981)
- (73) Eiermann H.J. et al., J. Am. Acad. Dermatol. 6, 909-917 (1982)
- (74) Fisher A.A. Contact Dermatitis, Lea & Febiger, Philadelphia, 3rd ed., 1986
- (75) Flyvholm M-A., Br. J. Indust. Med. 50, 1043-1050 (1993)
- (76) Flyvholm M-A., Contact Dermatitis 25, 49-56 (1991)
- (77) Fregert S. et al., J. Allergy 34, 404-408 (1963)
- (78) Frosch P.J., Ch. Raulin, Hautarzt 38, 331-334 (1987)
- (79) Green C., J.G. Lowe, Contact Dermatitis 27, 261 (1992)
- (80) Guimaraens D. et al., Contact dermatitis 35, 254 (1996)
- (81) Hirand Sh., K. Yoshikawa, Contact Dermatitis 8, 48-50 (1982)

- (82) Huwyler T., Schweiz. Rundschau Med. (Praxis) 80, 1183-1189 (1991)
- (83) Li m., E. Gow, Australian J. Dermatol. 36, 219-220 (1995)
- (84) Lodi A. et al., Contact Dermatitis 29, 281-282 (1993)
- (85) Marren P., F. Wojnarowska, Seminars in Dermatology 15, 36-41 (1996)
- (86) Mosca M. et al., Chronica dermatologica 5, 585-594 (1995)
- (87) Scheman A.J., R. Katta, Contact Dermatitis 37, 130 (1997)
- (88) Schubert H., E. Prater, Zeitschr. Hautkr. 67, 330-333 (1992)
- (89) Wurbach G. et al., Contact Dermatitis 28, 187-188 (1993)
- (90) Opdyke, D. L.: J.: Fd. Cosmet. Toxicol. 11, 1011-1013 (1973)
- (91) Carpenter, C. P. et al.: J. Ind. Hyg. Toxicol. 31, 343-346 (1949)
- (92) BIBRA: Toxicity Profile Benzyl Alcohol (1989)
- (93) Florin, I. et al.: Toxicology 15, 219-232 (1980)
- (94) Milvy, P., Garro, A. J.: Mutat. Res. 40, 15-18 (1976)
- (95) Mortelmans, K. et al.: Environ. Mutagen. 8, Suppl. 7, 1-119 (1986)
- (96) Zeiger, E. et al., Environ. Mutagen. Molec. Mutagen. 16 (Suppl. 18), 1-14 (1990)
- (97) Rogan, E. G. et al.: Chem.-Biol. Interactions 58, 253-275 (1986)
- (98) Ishidate, M. et al.: Fd. Chem. Toxic. 22, 623-636 (1984)
- (99) Wiessler, M. et al.: Carcinogenesis 4, 867-871 (1983)
- (100) Ball, J. C. et al.: Mutat. Res. 138, 145-151 (1984)
- (101) Kuroda, K. et al.: Mutat. Res. 130, 369 (1984)
- (102) Yoo, Y. S.: Osaka-shi Igakkai Zasshi 34, 267-288 (1985)
- (103) Anderson B.E. et al., Environm. Molec. Mutagen. 16 [Suppl 18] 55-137 (1990)
- (104) Ishidate, M. et al.: Mutat. Res. 195, 151-213 (1988)

- (105) McGregor, D. B. et al.: Environ. Mutagen. 12, 85-154 (1988)
- (106) Myhr B. et al., Environm. Molec. Mutagen. 16, [Suppl 18], 138-167 (1990)
- (107) Elia M.C. et al., Environm. Molec. Mutagen. 24, 181-191 (1994)
- (108) Storer R.D. et al., Mutat. Res. 368, 59-101 (1996)
- (109) Fluck, E. R. et al.: Chem.-Biol. Interactions 15, 219-231 (1976)
- (110) Leifer Z. et al., Mutat. Res. 87, 211-297 (1981)
- (111) Matthews E. J., Environm. Health Perspec. 101 [Suppl 2], 347-482 (1994)
- (112) Foureman P. et al., Environm. Molec. Mutagen. 23, 208-227 (1994)
- (113) Hayashi, M. et al.: Fd. Chem. Toxic. 26, 487-500 (1988)
- (114) Uno Y. et al., Mutat. Res. 320, 189-205 (1994)
- (115) Miyagawa M. et al., Mutat. Res. 343, 157-183 (1995)
- (116) Dieter M.P., Govt Reports Announcement & Index (GRA&I), Issue 02, 1990
- (117) Miller, C.E. et al., Cancer Res. 43, 1124-1134 (1983)
- (118) Hardin, B. D. et al.: Teratog. Carcinog. Mutagen. 7, 29-48 (1987)
- (119) Hazelden et al., 1983, cited in: BIBRA: Toxicity Profile Benzyl Alcohol (1989)
- (120) Duraiswami, P. K.: Bull. John Hopkins Hosp. 95, 57-67 (1954)
- (121) York R.G. et al., Teratology 37, 503-504 (1988)
- (122) Bray, H. G. et al.: Biochem. J. 48, 88-96 (1951)
- (123) Bray, H. G. et al.: Biochem. J. 70, 570-579 (1958)
- (124) Diack, S. L., Lewis, H. B.: J. Biol. Chem. 77, 89-95 (1928)
- (125) Patty's Industrial Hygiene and Toxicology, Vol. 2C, 4640-4641, John Wiley and Sons, New York (1982)
- (126) Snapper, J. et al.: Biochem. Z. 155, 163-173 (1924-1925)

- (127) Stekol, J. A.: J. Biol. Chem. 128, 199-205 (1939)
- (128) Williams, R. T.: Detoxification Mechanisms, Chap. 10, 318-347 John Wiley and Sons Inc. New York (1959)
- (129) Watanabe S., Pharmacometrics 47, 177-198 (1994)
- (130) Koch H.P. et al., Meth. Find Exp. Clin. Pharmacol. 15, 141-153 (1993)
- (131) Koch H.P., Pharmazie 47, 531-537 (1992)
- (132) Messiha F.S. et al., Pharmacol. Biochem. Behavior 43, 1071-1074 (1992)
- (133) Messiha F.S., Comp. Biochem. Physiol c 99, 445-449 (1991)
- (134) Messiha F.S., Res. Commun. Subst. Abuse 13, 123-126 (1992)
- (135) Shearer G.L. et al., Biochemistry 32, 11186-11194 (1993)
- (136) Radwan M., Dug Develop. Indust. Pharm. 20, 2753-2762 (1992)
- (137) Tamaoki J. et al., Am. J. Physiol. 258, L355-L360 (1990)
- (138) DeLand, F. H.: Toxicol. Appl. Pharmacol. 25, 153-156 (1973)
- (139) Baker, N., Huebotter, R. J.: Life Sciences 10, 1193-1199 (1971)
- (140) Ballowitz, L. et al.: J. Perinat. Med. 4, 168-183 (1976)
- (141) Ballard, H. J. et al.: Comp. Biochem. Physiol. 90A, 807 (1988)
- (142) Ballard, H. J. et al.: Gut 29, 1648-1655 (1988)
- (143) Bronaugh, R. L. et al.: Fd. Chem. Toxic. 28, 369-373 (1990)
- (144) Buck, K. J. et al.: Eur. J. Pharmacol. 160, 359-367 (1989)
- (145) Ansel, H. C., Cadwallader, D. E.: J. Pharm. Sci. 53, 169-172 (1964)
- (146) McOrmond, P. et al.: Drug Intell. Clin. Pharm. 14, 549 (1980)
- (147) Atkinson, J. P. et al.: J. Clin. Invest. 60, 284-294 (1977)
- (148) Chazotte, B., Vanderkool, G.: Biochim. Biophys. Acta 636, 153- 161 (1981)

- (149) Cullison, R. F.: J. Am. Vet. Med. Ass. 182, 61 (1983)
- (150) Dudeja, P. K. et al.: Am. J. Physiol. 257, G809-G817 (1989)
- (151) Duncan, D., Jarvis W. H.: Anaesthesia 4, 465-474 (1943)
- (152) Eichbaum, F. W., Yasaka, W. J.: Basic Res. Cardiol. 71, 355-370 (1976)
- (153) Macmillan, K. L. et al.: Aust. Vet. J. 49, 267-268 (1973)
- (154) Pietrzak, J. et al.: Pharmacology 39, 265-272 (1989)
- (155) Sollmann, T.: J. Pharmac. exp. Ther. 13, 355-360 (1919)
- (156) Scher, W. et al.: J. Biol. Regul. Homeost. Agents 3, 91-97 (1989)
- (157) Sainte-Marie, J. et al.: FEBS Lett. 262, 13-16 (1990)
- (158) Watanabe, M. et al.: Hokuriku Koshu Eisei Gakkaishi 9, 12-17 (1982)
- (159) Kim, J. et al.: Pediatr. Res. 27, 61A (1990)
- (160) LeBel, M. et al.: Dev. Pharmacol. Ther. 11, 347-356 (1988)
- (161) Kassam, J. P. et al.: Drug Metab. Dispos. 17, 567-572 (1989)
- (162) Coles, W.H. (1975) cited in: Grant, W.M. and Glending, D., toxicology of the eye, third edition, Charles C. Thomas, publisher, Springfield, Ill./USA
- (163) Messiha F.S. et al., Pharmacol. Commun. 1,53-57 (1992)
- (164) Montaguti P. et al., Arzneim.-Forsch (Drug Res.) 44, 566-570 (1994)
- (165) Anderson, C. W. et al.: Am. J. Obstet. Gynecol. 148, 344-346 (1984)
- (166) Brown, W. J. et al.: Lancet 1, 1250 (1982)
- (167) Gershanik, J. et al.: Clin. Res. 29, 895A (1981)
- (168) Gershanik, J. et al.: New Engl. J. Med. 307, 1384-1388 (1982)
- (169) Hiller, J. L. et al.: Pediatrics 77, 500-506 (1986)
- (170) Jardine, D. S., Roger, K.: Pediatrics 83, 153-160 (1989)

- (171) Lovejoy, F. H.: *Am. J. Dis. Child.* 136, 974-975 (1982)
- (172) Santeiro, M. L.: *Fl. J. Hosp. Pharm.* 9, 17-19 (1989)
- (173) Novak, E. et al.: *Toxicol. Appl. Pharmacol.* 23, 54-61 (1972)
- (174) Addo, H. A. et al.: *Br. J. Dermatol.* 107, 261-274 (1982)
- (175) Fisher, A. A.: *Contact Dermatitis* 1, 281-284 (1975)
- (176) Fregert, S., Hjorth, N.: *Contact Dermatitis Newsletter* 5, 85-86 (1969)
- (177) Grant, J. A. et al.: *New Engl. J. Med.* 306, 108 (1982)
- (178) Lagerholm, B. et al.: *Acta allergologica* 12, 295-298 (1958)
- (179) Larsen, W. G.: *Arch. Dermatol.* 113, 623-626 (1977)
- (180) Larsen, W. G.: *J. Am. Acad. Dermatol.* 21, 880-884 (1989)
- (181) Lazzarini, S.: *Contact Dermatitis* 8, 349 (1982)
- (182) Schultheiss, E.: *Derm. Wschr.* 135, 629-633 (1957)
- (183) Shmunes, E.: *Arch. Dermatol.* 120, 1200-1201 (1984)
- (184) Shoji, A.: *Contact Dermatitis* 9, 510 (1983)
- (185) Wilson, J. P. et al.: *Drug Intell. Clin. Pharm.* 20, 689-691 (1986)
- (186) De Groot, A. C. et al.: *Contact Dermatitis* 15, 218-222 (1986)
- (187) Reynolds, P., Wilton, N.: *Anesth. Analg.* 69, 855-856 (1989)
- (188) Weissmann, D. E., Rockoff, M. A.: *Anesth. Analg.* 70, 673-674 (1990)
- (189) Bowen D. et al., *Clinica Chimica Acta* 61, 399-401 (1975)
- (190) Testa M. et al., *J. Ocular Pharmacol.* 3, 211-225 (1987)
- (191) Williams J.M., N.R. Howe, *J. Dermatol. Surg. Oncol.* 20, 730-733 (1994)
- (192) Ahlfors C.E, G.R. Kaleem, *Pediatric Res.* 37, 192 A (1994)
- (193) *Am. Acad. Pediatrics: Committee on Drugs, Pediatrics* 99, 268-278 (1997)

- (194) Benda G.I. et al., Pediatrics 77, 507-512 (1986)
- (195) Cronin C.M. et al., Am. J. Perinatol. 8, 80-85 (1991)
- (196) Cronin C.M.G., Pediatrics 89, 1129-1130 (1992)
- (197) Ellenhorn M.J., Barceloux D.G., Medical Toxicology, diagnosis and treatment of human poisoning, Elsevier, New York, Amsterdam, London, 1988, p. 528
- (198) Little G.A. et al., Pediatrics 72, 356-358 (1982)

**7.1 Risk Assessment**

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