

201-14921B

# I U C L I D

# Data Set

Existing Chemical ID: 107-18-6  
CAS No. 107-18-6  
EINECS Name allyl alcohol  
EC No. 203-470-7  
TSCA Name 2-Propen-1-ol  
Molecular Formula C3H6O

Producer Related Part  
Company: Lyondell Chemical Co.  
Creation date: 01-SEP-2003

Substance Related Part  
Company: Lyondell Chemical Co.  
Creation date: 01-SEP-2003

Memo: AA HPV dataset

Printing date: 25-NOV-2003  
Revision date:  
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Reliability (profile): Reliability: without reliability, 1, 2, 3, 4  
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(DE), TA-Luft (DE), Material Safety Dataset, Risk  
Assessment, Directive 67/548/EEC, SIDS

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**1.0.1 Applicant and Company Information**

Name: Lyondell Chemical Co.  
Contact Person: Dr Marcy I Banton Date:  
Street: One Houston Center, Suite 1600, 1221 McKinney Street  
Town: Houston, Texas TX 77010  
Country: United States

25-NOV-2003

**1.0.2 Location of Production Site, Importer or Formulator**

**1.0.3 Identity of Recipients**

**1.0.4 Details on Category/Template**

**1.1.0 Substance Identification**

Mol. Formula: C3H6O  
Mol. Weight: 58.08

07-NOV-2003

**1.1.1 General Substance Information**

Purity type: typical for marketed substance  
Substance type: organic  
Physical status: liquid  
Purity: >= 99 - % w/w  
Colour: clear, colorless  
Odour: sharp, mustard-like

25-NOV-2003

(25) (26)

**1.1.2 Spectra**

**1.2 Synonyms and Tradenames**

propenol, 1-propen-3-ol, vinyl carbinol, 3-hydroxypropene, 2-propen-1-ol,  
2-propenyl alcohol.

11-NOV-2003

(25)

### 1.3 Impurities

**Purity type:** typical for marketed substance

**Remark:** Typical impurities:  
n-propanol 0.75% w/w max  
water 0.30% w/w max  
propionaldehyde 0.01% w/w max

25-NOV-2003

(25)

### 1.4 Additives

### 1.5 Total Quantity

**Remark:** Allyl alcohol (CAS 107-18-6) is an intermediate chemical manufactured by Lyondell Chemical Company at sites in the U.S. and The Netherlands. Projected global production is estimated at 175 million pounds. Approximately 140 million pounds will be used captively by Lyondell for manufacture of downstream derivatives.

Allyl alcohol is also produced in Asia mainly by two Japanese producers, Showa Denka and Daicel. Estimated total Asian production is about 125 million pounds.

25-NOV-2003

### 1.6.1 Labelling

### 1.6.2 Classification

### 1.6.3 Packaging

### 1.7 Use Pattern

**Remark:** Allyl Alcohol is an isomer of propylene oxide, and is a bifunctional molecule used by chemical manufacturers for a multitude of purposes by reaction of the alkene functionality, the hydroxy functionality, or both.

A significant use for Allyl Alcohol is as an intermediate in the production of 1,4-Butanediol (CAS 110-63-4) and 2-Methyl-1,3-Propanediol (CAS 2163-42-0). Other commercial

uses of allyl alcohol include manufacture of allyl diglycol carbonate (CAS 142-22-3), used in optical resins; allyl glycidyl ether (CAS 106-92-3) used as silane coupling agents for a multitude of applications, such as water treatment and glass adhesion, diallyl phthalate (CAS 131-17-9), which may be used as a plasticizer, and allyl methacrylate (CAS 96-05-9) and styrene allyl alcohol (CAS 25119-62-4) resins for coatings applications.

25-NOV-2003

**1.7.1 Detailed Use Pattern****1.7.2 Methods of Manufacture****1.8 Regulatory Measures****1.8.1 Occupational Exposure Limit Values**

Remark:	Occupational exposure limits:				
	Source/Data	ppm	mg/m <sup>3</sup>	-- Type --	-- Notation --
	US (ACGIH)/2001	0.5	1.19	8 hr TWA	Skin (Carc, N/L)
	MAK (AT)/1994	2	5	8 hr TWA	Skin
		4	10	30 min STEL	Skin
	OEL (BE)/2000	2	4.9	8 hr TWA	Skin
		4	9.6	15 min STEL	Skin
	MAK (DA)/1996	2	5	8 hr TWA	Skin
	ELV (FI)/1998	2	4.8	8 hr TWA	Skin
		4	9.6	15 min STEL	Skin
	INRS (FR)/1999	2	5	8 hr TWA	Skin
		4	9.6	15 min STEL	Skin
	TRGS 900/2000	2	4.8	8 hr TWA	Skin
		4	9.6	15 min STEL	Skin
	ELV (IE)/1999	2	5	8 hr TWA	Skin
		4	10	15 min STEL	Skin
	OEL (IT)/1999	2	4.8	8 hr TWA	Skin
		5	12.1	15 min STEL	Skin

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MAC (NL)/2000	2	5	8 hr TWA	Skin
ELV (NO)/1996	2	5	8 hr TWA	Skin, Sen
VAL (ES)/2000	0.5	1.2	8 hr TWA	Skin
TLV (SE)/2000	2	5	8 hr TWA	Skin
	6	14	15 min STEL	Skin
SUVA/1999	2	5	8 hr TWA	Skin
	4	10	15 min STEL	Skin
EH40 (OES)/2000	2	4.8	8 hr TWA	Skin
	4	9.7	15 min STEL	Skin

25-NOV-2003

(25)

**1.8.2 Acceptable Residues Levels**

**1.8.3 Water Pollution**

**1.8.4 Major Accident Hazards**

**1.8.5 Air Pollution**

**1.8.6 Listings e.g. Chemical Inventories**

**1.9.1 Degradation/Transformation Products**

**1.9.2 Components**

**1.10 Source of Exposure**

**1.11 Additional Remarks**

1. General Information

date: 25-NOV-2003  
Substance ID: 107-18-6

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**1.12 Last Literature Search**

**1.13 Reviews**

### 2.1 Melting Point

**Value:** = -129 degree C

**Test substance:** Described as allyl alcohol; no further information available.

**Reliability:** (2) valid with restrictions

Secondary literature (handbook or compilation of data)

03-NOV-2003

(13) (20) (38)

### 2.2 Boiling Point

**Value:** = 97 degree C

**Test substance:** Described as allyl alcohol; no further information available.

**Reliability:** (2) valid with restrictions

Secondary literature (handbook or compilation of data)

03-NOV-2003

(39)

**Value:** = 96.9 degree C

**Test substance:** Described as allyl alcohol; no further information available.

**Reliability:** (2) valid with restrictions

Secondary literature (handbook or compilation of data)

03-NOV-2003

(38)

### 2.3 Density

**Type:** density

**Value:** = .854 g/cm<sup>3</sup>

**Test substance:** Described as allyl alcohol; no further information available.

**Reliability:** (2) valid with restrictions

Secondary literature (handbook or compilation of data)

03-NOV-2003

(39) (40)

**Type:** density

**Value:** = .825 g/cm<sup>3</sup>

**Test substance:** Described as allyl alcohol; no further information available.

**Reliability:** (2) valid with restrictions

Secondary literature (handbook or compilation of data)

03-NOV-2003

(38)

#### 2.3.1 Granulometry

### 2.4 Vapour Pressure

**Remark:** Vapor Pressure = 26.1 mm Hg (experimental)  
Equivalent to 3,480 Pa.  
**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (2) valid with restrictions  
Secondary literature (handbook or compilation of data)  
03-NOV-2003 (9)

**Remark:** 23.8 mm Hg at 25 degrees C  
**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (2) valid with restrictions  
Secondary literature (handbook or compilation of data)  
03-NOV-2003 (39)

**Remark:** 20 mm Hg at 20 degrees C  
32 mm Hg at 30 degrees C  
**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (2) valid with restrictions  
Secondary literature (handbook or compilation of data)  
03-NOV-2003 (38)

**Remark:** 23.5 mm Hg at 25 degrees C  
**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (2) valid with restrictions  
Secondary literature (handbook or compilation of data)  
03-NOV-2003 (13)

### 2.5 Partition Coefficient

**Partition Coeff.:** octanol-water  
**log Pow:** = .17

**Remark:** Method described as 'direct'.  
**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (2) valid with restrictions  
Secondary literature (handbook or compilation of data)  
03-NOV-2003 (13) (33) (38)

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**Partition Coeff.:** octanol-water  
**log Pow:** = -.25

**Remark:** CLOGP3 calculation

Method: Leo and Weininger (1985) Medchem Software Release  
3.33, Medicinal Chemistry Project, Pomona College, Claremont,  
CA.

**Test substance:** Described as allyl alcohol; no further information available.

**Reliability:** (2) valid with restrictions  
Secondary literature

03-NOV-2003

(23)

### 2.6.1 Solubility in different media

**Solubility in:** Water

**Result:** Water solubility = 1E+006 g/m<sup>3</sup> (experimental)

**Test substance:** Described as allyl alcohol; no further information available.

**Reliability:** (2) valid with restrictions  
Secondary literature (handbook or compilation of data)

03-NOV-2003

(9)

**Solubility in:** Water

**Remark:** Described as miscible;

Constant boiling mixture (BpT 87.5 degrees C) formed from  
72.3% allyl alcohol + 27.7% water

**Test substance:** Described as allyl alcohol; no further information available.

**Reliability:** (2) valid with restrictions  
Secondary literature (handbook or compilation of data)

03-NOV-2003

(40)

**Solubility in:** Water

**Remark:** Described as miscible.

**Test substance:** Described as allyl alcohol; no further information available.

**Reliability:** (2) valid with restrictions  
Secondary literature (handbook or compilation of data)

03-NOV-2003

(13)

### 2.6.2 Surface Tension

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**2.7 Flash Point**

**Value:** = 21.1 degree C  
**Type:** open cup

**Remark:** Reported as 70 degrees F (open cup).  
**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (2) valid with restrictions  
Secondary literature (handbook or compilation of data)  
03-NOV-2003 (40)

**Value:** = 23.9 degree C  
**Type:** closed cup

**Remark:** Reported as 75 degrees F (closed cup).  
**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (2) valid with restrictions  
Secondary literature (handbook or compilation of data)  
03-NOV-2003 (40)

**Value:** = 21 degree C

**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (2) valid with restrictions  
Secondary literature (handbook or compilation of data)  
03-NOV-2003 (39)

**2.8 Auto Flammability**  
-**2.9 Flammability**  
-**2.10 Explosive Properties**  
-**2.11 Oxidizing Properties**  
-**2.12 Dissociation Constant**  
-**2.13 Viscosity**  
-

**3.1.1 Photodegradation**

**Type:** air

**Year:** 1993

**Remark:** Study examined atmospheric oxidation of allyl alcohol. Carbonyl products of reaction of allyl alcohol with ozone and cyclohexane, isolated as their 2,4-dinitrophenyl hydrazones, were determined using HPLC analysis (cyclohexane added to scavenge OH; reaction carried out in the dark in purified, humid air). Carbonyl products' presence confirmed using 430/360 nm absorbance ratio; quantitation involved use of external standards and construction of calibration curves.

**Result:** Carbonyl products of reaction of allyl alcohol with ozone were formaldehyde (average molar yield  $0.50 \pm 0.03$ ), hydroxyacetaldehyde (average molar yield  $0.30 \pm 0.03$ ), and an unidentified monofunctional carbonyl formed in low yield.

**Test substance:** Described as allyl alcohol; no further information available.

**Reliability:** (2) valid with restrictions  
Study available for review. Experimental study. Reasonably well reported methods and results, suitable for assessment.

05-NOV-2003 (11)

**Type:** air

**Light source:** other: high pressure mercury vapor lamp

**Light spect.:** = 230 - 300 nm

**Method:** 100 ppm allyl alcohol vapor irradiated with light source in glass chamber. Degradation products (CO<sub>2</sub> and CO) measured using nondispersive IR gas chromatography and gas chromatography on a molecular sieve using an ultrasound detector, respectively.

**Result:** No photolysis occurred at wavelengths > 300 nm. At wavelengths between 230 nm and 300 nm, 39.7 % of the initial concentration of allyl alcohol was broken down into CO<sub>2</sub> and CO after 2 hrs of illumination. The concentrations of CO<sub>2</sub> and CO after 2 hrs of illumination were 32 ppm and 87 ppm.

**Test substance:** Described as allyl alcohol; no further information available.

**Conclusion:** No photolysis is expected to occur in troposphere.

**Reliability:** (2) valid with restrictions  
Study available for review. Experimental study. Reasonably well reported methods and results, suitable for assessment.

31-OCT-2003 (16)

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**Type:** air

**Year:** 1993  
**GLP:** no data

**Remark:** Study examined kinetics of gas-phase reaction of ozone with allyl alcohol investigated at atmospheric pressure, ambient temperature, and in presence of cyclohexane to scavenge hydroxyl radicals produced during reaction.

Initial allyl alcohol concentration of 1.75 - 2.0 ppm, initial ozone concentrations of 174 - 200 ppb and cyclohexane concentrations of 200 or 400 ppm. Ozone was monitored continuously by ultraviolet photometry. Reaction rate constant for allyl alcohol, corrected for the measured loss of ozone to the chamber walls, was  $14.4 \pm 2.0 \text{ E-18 cm}^3/\text{molecule}/\text{sec}$ .

Hydroxyl radicals reaction:  
Overall OH rate constant =  $2.59 \text{ E-11 cm}^3/\text{molecule-sec}$   
Removal by OH half-life = 0.31 days or 7.44 hr ( $1.0 \text{ E6 OH}/\text{cm}^3$ )

Removal by ozone half-life = 0.23 days or 5.52 hr (100 ppb ozone)

**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (2) valid with restrictions  
Study available for review. Experimental study. Reasonably well reported methods and results, suitable for assessment.

18-NOV-2003 (12)

**Type:** other

**Year:** 1991  
**GLP:** no data

**Remark:** Photoxidation half life, water = 334 d to 37 yr

Basis: "Based upon measured rate constant for reaction with hydroxyl radical in water."

Photoxidation half life, air = 2.2-22 hr

Basis: "Scientific judgement based upon estimated rate constant with hydroxyl radical in air."

**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (2) valid with restrictions  
Secondary literature (handbook or compilation of data)

31-OCT-2003 (14)

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**Type:** other

**Year:** 1989  
**GLP:** no data

**Remark:** Release of allyl alcohol to the atmosphere is expected to result mainly in reaction with photochemically generated hydroxyl radicals with estimated half lives of 6.03-14.7 hr.

**Test substance:** Described as allyl alcohol; no further information available.

**Reliability:** (2) valid with restrictions  
Secondary literature (handbook or compilation of data)

31-OCT-2003 (13)

### 3.1.2 Stability in Water

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### 3.1.3 Stability in Soil

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### 3.2.1 Monitoring Data (Environment)

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### 3.2.2 Field Studies

-

### 3.3.1 Transport between Environmental Compartments

**Type:** fugacity model level I

**Method:** other: Level 1 Mackay Fugacity Model Version 2.11, August 1999  
from <http://www.trentu.ca/cemc/models.html>.

**Method:** INPUT DATA:  
Molecular weight = 58.08  
Data temperature = 25 degrees C  
Log Kow = 0.17 (experimental)  
Water solubility = 1E+006 g/m<sup>3</sup> (experimental)  
Vapour pressure = 3,480 Pa (experimental)  
Melting point = -129 degrees C (experimental)

**Result:** The percentage environmental distribution calculated from the above parameters using the MacKay level 1 model was as follows:

Air	3.9119%
Soil	0.1257%
Water	95.9596%
Fish	7.10E-06%
Sediment	0.0028%
Suspended Sediment	8.73E-05%
Aerosol	1.35E-07%

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**Reliability:** (2) valid with restrictions  
Study performed according to accepted principles using USEPA recommended model.  
21-NOV-2003 (2)

**Type:** fugacity model level III  
**Method:** other: Level 1 Mackay Fugacity Model Version 2.11, August 1999 from <http://www.trentu.ca/cemc/models.html>.

**Method:** The Level III program was also used, with the default model, using the same input parameters given in the preceding record.

**Remark:** The distribution between compartments obtained was as follows:

Release:	To air	To water	To soil
% in air	71.5%	0.0426%	0.151%
% in soil	12.4%	0.0074%	79.6%
% in water	16.1%	99.8%	20.2%
% in sediment	0.0276%	0.171%	0.0346%

The results reflect that most allyl alcohol released to the air would remain in the air. In water, allyl alcohol is not expected to sorb to sediment. If released to the soil, allyl alcohol is likely to remain in the soil.

**Reliability:** (2) valid with restrictions  
Study performed according to accepted principles using USEPA recommended model.  
21-NOV-2003 (2)

### 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:** other: settled sewage seed  
**Concentration:** 2.5 µg/l related to Test substance  
**Kinetic:** 5 day(s) = 9 %  
10 day(s) = 55 %  
15 day(s) = 78 %  
20 day(s) = 82 %

**Year:** 1989  
**GLP:** no data

**Remark:** Results presented as percentage theoretical BOD.  
**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (2) valid with restrictions  
Secondary literature (handbook or compilation of data)  
21-NOV-2003 (13)

**Type:** aerobic

**Year:** 1992  
**GLP:** no data

**Method:** Sludge: 30 mg/l  
Substance: 100 mg/l  
Period 2 wk  
(No further details)

**Result:** 86% degradation by BOD  
**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (2) valid with restrictions  
Secondary literature (handbook or compilation of data)  
18-NOV-2003 (20)

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**Type:** aerobic

**Year:** 1995  
**GLP:** no data

**Method:** ORIGIN OF SAMPLE  
Sediment and water was collected from Kern County Canal, an irrigation canal in an agricultural region of California, USA. Sediment was sandy loam with 0.5% organic matter.

DEGRADATION TEST  
1:2 sediment to water ratio in 2 Erlenmeyer flasks fitted with Dreschel caps with inlet and outlet ports for air (aerobic biodegradation test). [14C]acrolein (15 mg/L) added using a gastight syringe to the water phase of each test system. Experiment carried out in dark at 25 ± 1°C. Each flask was connected to a series of trapping vessels to collect biodegradation products: one Tenax trap to collect volatile products and two 1.0 N NaOH traps to collect [14C]CO<sub>2</sub>.

ANALYTICAL METHODS  
Three HPLC-RAM methods were used to separate acrolein and its degradation products in the water, sediment, and the traps: ion exchange chromatography, reversed phase chromatography, and anion-exchange chromatography. Liquid scintillation counting was used to confirm HPLC-RAM recoveries. Analytical reference standards included oxalic acid, malonic acid, glyceric acid, glyceraldehyde, glycidol, allyl alcohol, aconitic acid, lactic acid, glycerol, 3-hydroxypropanal, 1,3-propanediol, acrylic acid, and acrolein.

**Remark:** Allyl alcohol was a transient breakdown product of acrolein. Propanol was a transient breakdown product of allyl alcohol. Oxalic acid was a stable breakdown product of allyl alcohol and propanol. Aerobic microbial biomass at the conclusion of study was 5 x 10<sup>7</sup> cfu/g sediment.

**Result:** [14C]acrolein was reduced to allyl alcohol, which was further degraded to oxalic acid and CO<sub>2</sub>.

**Test substance:** Radiolabeled [2,3-<sup>14</sup>C] acrolein, lot 032H9223, specific activity 16.4 mCi/mmol from Sigma. Radiochemical purity 92.2% (HPLC).

**Conclusion:** Under aerobic test conditions, allyl alcohol was degraded by sediment microorganisms.

**Reliability:** (2) valid with restrictions  
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

15-NOV-2003

(35)

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**Type:** anaerobic

**Year:** 1995  
**GLP:** no data

**Method:** ORIGIN OF SAMPLE  
Sediment and water was collected from Kern County Canal, an irrigation canal in an agricultural region of California, USA. Sediment was sandy loam with 0.5% organic matter.

DEGRADATION TEST  
1:2 sediment to water ratio in 2 Erlenmeyer flasks fitted with Dreschel caps with inlet and outlet ports for nitrogen (anaerobic biodegradation test) exchange. [14C]acrolein (15 mg/L) added using a gastight syringe to the water phase of each test system. Experiment carried out in dark at 25 ± 1°C. Each flask was connected to a series of trapping vessels to collect biodegradation products: one Tenax trap to collect volatile products and two 1.0 N NaOH traps to collect [14C]CO<sub>2</sub>.

Analytical methods  
Three HPLC-RAM methods were used to separate acrolein and its degradation products in the water, sediment, and the traps: ion exchange chromatography, reversed phase chromatography, and anion-exchange chromatography. Liquid scintillation counting was used to confirm HPLC-RAM recoveries. Analytical reference standards included oxalic acid, malonic acid, glyceric acid, glyceraldehyde, glycidol, allyl alcohol, aconitic acid, lactic acid, glycerol, 3-hydroxypropanal, 1,3-propanediol, acrylic acid, and acrolein.

**Remark:** Allyl alcohol was a transient breakdown product of acrolein. Propanol was a transient breakdown product of allyl alcohol. Oxalic acid was a stable breakdown product of allyl alcohol and propanol. Anaerobic microbial biomass at the conclusion of the study was 3 x 10<sup>7</sup> cfu/g sediment.

**Result:** Under anaerobic aquatic conditions, [14C]acrolein was reduced to allyl alcohol, which was further degraded to propanol and ultimately to oxalic acid and CO<sub>2</sub>.

**Test substance:** Radiolabeled [2,3-<sup>14</sup>C] acrolein, lot 032H9223, specific activity 16.4 mCi/mmol from Sigma. Radiochemical purity 92.2% (HPLC).

**Conclusion:** Under anaerobic test conditions, allyl alcohol was degraded by sediment microorganisms.

**Reliability:** (2) valid with restrictions  
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

**3.6 BOD5, COD or BOD5/COD Ratio**

**Method:** other: APHA Standard Method No 219 (1971)  
**Year:** 1979  
**GLP:** no  
**Method:** other: ASTM D 1252-67 (1974)  
**Year:** 1979  
**GLP:** no  
**Method:** BOD  
 Tests were conducted in accordance with the standard dilution method of APHA at 20 degrees C for 5 d. Allylthiourea (0.5 mg/l) was added to inhibit nitrification. Filtered effluent (10 ml; unadapted) from a waste water treatment plant was used as inoculum, in a total volume of 500 ml. Glucose and glutamic acid were run in parallel as control substances. (No further details)

COD  
 Tests were performed in accordance with the standard potassium dichromate method described by ASTM. (No further details)

ThOD  
 Theoretical oxygen demand was obtained by calculation. (No further details)

**Result:** ThOD = 2.21 g/g  
 BOD = 1.79 g/g (81% of ThOD)  
 COD = 2.12 (96% of ThOD)

**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (2) valid with restrictions  
 Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

22-OCT-2003 (3)  
**Method:** other: standard dilution method  
**Year:** 1955  
**GLP:** no  
**Year:**

**Method:**  
**Remark:** BOD (10 d) = 1.6 g/g (using sewage seed)

Source reference: Mills, EJ and Stack, VT jr (1953) Biological oxidation of synthetic organic chemicals. Proceedings of the 8th Purdue Industrial Waste Conference (1953), p 492 (Unavailable for review)

**Reliability:** (2) valid with restrictions  
 Secondary literature

22-OCT-2003 (15)

**3.7 Bioaccumulation**

**Species:** other: predicted value  
**BCF:** = 3.16

**Remark:** METHOD  
BCFWin v2.14 in EPIWin v3.10 from the USEPA and Syracuse Research Corporation, as described by Meylan et al. (1999).

INPUT DATA  
CAS No. 107-18-6  
Log Kow = 0.17 (from EPIWin experimental database)

**Conclusion:** RESULTS  
Estimated BCF = 3.162 (log BCF = 0.500)  
Allyl alcohol is not likely to bioaccumulate.  
**Reliability:** (2) valid with restrictions  
Study performed according to accepted principles using USEPA recommended model.

18-NOV-2003

(1) (9) (28)

**3.8 Additional Remarks**

**Memo:** Predicted half-life in air

**Remark:** Predicted air half life = 2.2-22 hr

**Reliability:** Basis: "Scientific judgment based upon estimated photooxidation half-life in air."  
(4) not assignable  
Secondary literature (handbook or compilation of data)

04-NOV-2003

(14)

**Memo:** Predicted half-life in surface water

**Remark:** Predicted surface water half life = 2-14 d

**Reliability:** Basis: "Scientific judgment based upon estimated unacclimated aqueous aerobic biodegradation half-life."  
(4) not assignable  
Secondary literature (handbook or compilation of data)

04-NOV-2003

(14)

**Memo:** Predicted aqueous half life (aerobic biodegradation)

**Remark:** Predicted aerobic half life (biodegradation) = 1-7 d

Basis: "Scientific judgment based upon estimated unacclimated aqueous aerobic biodegradation screening test data."

Removal/secondary treatment = 73%

**Reliability:** Basis: "Based upon biological oxygen demand results from activated sludge dispersed seed aeration treatment simulator."  
(4) not assignable  
Secondary literature (handbook or compilation of data)  
04-NOV-2003 (14)

**Memo:** Predicted aqueous half life (anaerobic biodegradation)

**Remark:** Predicted anaerobic half life (biodegradation) = 4-28 d

**Reliability:** Basis: "Scientific judgment based upon estimated unacclimated aqueous aerobic biodegradation half life."  
(4) not assignable  
Secondary literature (handbook or compilation of data)  
04-NOV-2003 (14)

**Memo:** Predicted half-life in soil

**Remark:** Predicted soil half life = 1-7 d

**Reliability:** Basis: "Scientific judgment based upon estimated unacclimated aqueous aerobic biodegradation rate."  
(4) not assignable  
Secondary literature (handbook or compilation of data)  
04-NOV-2003 (14)

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

**Type:** static  
**Species:** Pimephales promelas (Fish, fresh water)  
**Exposure period:** 96 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**LC50:** = .32 - calculated

**Year:** 1986  
**GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** EXPOSURE CONDITIONS  
Static multi-species bioassays were performed in seamless Pyrex glass vessels (30.5 x 30.5 x 30.5 cm) containing 20 l test solution. Water (industrial service water, Lake Ontario) was active-carbon-filtered, dechlorinated and tempered before use; total hardness 130 mg/l; pH 7.4 (detailed chemical composition provided). If the dissolved oxygen fell below 40% of the starting level (not reported), the test was re-run with glass sparger aeration (0.05 l/min).

Organisms were exposed to nominal concentrations of 0, 0.1, 1, 10 or 100 mg allyl alcohol/l test medium.

GENERAL TEST METHOD  
This non-standard test method simultaneously exposed 7 organisms (pillbug, water flea, flatworm, sideswimmer, snail, segmented worm, fathead minnow) to the test substance. Fish and snails were placed free in the tanks. The remaining organism were segregated in stainless steel wirecloth basket (5.5 cm diameter x 7.5 cm depth) suspended around the circumference of the vessel (baskets raised and lowered in the water column at 1 rpm). Total biological loading (all species combined) was 0.5 g/l test medium. The water temperature during the test was 20 degrees, with a 16 hr photoperiod. Each test was performed twice.

TEST ORGANISMS  
Fathead minnow (Pimephales promelas), approx. 0.2-0.5 g (10 per exposure concentration). The fish were acclimated to control diluent water in breeding/rearing tanks, and food withheld for 24 hr preceding the test.

PHYS-CHEM PARAMETERS  
Water temperature, dissolved oxygen and pH were recorded daily (but not reported).

BIOLOGICAL OBSERVATIONS  
Survival, condition and behavior were recorded daily. Dead organisms were removed when observed. All species were exposed for 96 hr. If during the test more than 5/10 of any one

species of test species were found dead, additional aquaria containing lower concentrations of test solution were set up.

## DETERMINATION OF LC50

LC50 values were calculated (computer model) based upon the log exposure concentration and the angle transformed percent mortality.

**Result:** Trial 1 LC50 = 0.32 mg/l

Trial 2 LC50 = 0.32 mg/l

**Test substance:** Described as allyl alcohol; no further information available.  
**Conclusion:** Under the conditions of this study (static conditions), the 96 hr LC50 for allyl alcohol in the fathead minnow (*Pimephales promelas*) was 0.32 mg/l.

**Reliability:** (2) valid with restrictions  
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

22-OCT-2003

(10)

**Type:** static  
**Species:** *Carassius auratus* (Fish, fresh water)  
**Exposure period:** 24 hour(s)  
**Unit:** mg/l **Analytical monitoring:** yes  
**LC50:** ca. 1 - calculated  
**Method:** other: APHA Method 231 (1971)  
**Year:** 1979  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** EXPOSURE CONDITIONS  
Groups of 6 goldfish (*Carassius auratus*, mean length 6.2 +/- 0.7 cm, mean weight 3.3 +/- 1.0 g) were placed in all glass tanks (42 x 28 x 28 cm) containing 25 l of tap water at 20 degrees C. The exposure lasted 24 hr.

Analysis of tap water was as follows (mg/l):

Cl<sup>-</sup>: 65  
NO<sub>2</sub><sup>-</sup>: 0  
NO<sub>3</sub><sup>-</sup>: 4  
SO<sub>4</sub><sup>2-</sup>: 35  
PO<sub>4</sub><sup>3-</sup>: 0.15  
HCO<sub>3</sub><sup>-</sup>: 25  
SiO<sub>2</sub>: 25  
NH<sub>4</sub><sup>+</sup>: 0  
Fe: 0.05  
Mn: 0  
Ca<sup>2+</sup>: 100  
Mg<sup>2+</sup>: 8  
alkali: 30 (as Na<sup>+</sup>)  
pH: 7.8

## ANALYSIS

The concentration of allyl alcohol in test medium was determined before and after each test, using either total organic carbon analysis or extraction/GC analysis (no further details). Comment: The concentration range used, and the recovery of added test substance, is not reported.

## DETERMINATION OF LC50

Results were obtained by interpolation after plotting log exposure concentration versus mortality.

Comment: The test medium was not aerated to avoid evaporative loss of the test substance. It is noted that the oxygenation concentration did not fall below 4 mg/l.

**Result:** 24 hr LC50 = 1 mg/l  
**Test substance:** Described as allyl alcohol; no further information available.  
**Conclusion:** Under the conditions of the test, the 24 hr LC50 of allyl alcohol in goldfish is 1 mg/l.  
**Reliability:** (2) valid with restrictions  
 Study available for review. Pre-guideline, non-GLP study investigation. Only limited information available but supports overall hazard assessment.

18-NOV-2003

(4)

**4.2 Acute Toxicity to Aquatic Invertebrates**

**Type:** static  
**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 96 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**EC50:** = .25 - .4 calculated

**Year:** 1986  
**GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** EXPOSURE CONDITIONS  
 Static multi-species bioassays were performed in seamless Pyrex glass vessels (30.5 x 30.5 x 30.5 cm) containing 20 l test solution. Water (industrial service water, Lake Ontario) was active-carbon-filtered, dechlorinated and tempered before use; total hardness 130 mg/l; pH 7.4 (detailed chemical composition provided). If the dissolved oxygen fell below 40% of the starting level (not reported), the test was re-run with glass sparger aeration (0.05 l/min).

Organisms were exposed to nominal concentrations of 0, 0.1, 1, 10 or 100 mg allyl alcohol/l test medium.

## GENERAL TEST METHOD

This non-standard test method simultaneously exposed 7 organisms (pillbug, water flea, flatworm, sideswimmer, snail, segmented worm, fathead minnow) to the test substance. Fish

and snails were placed free in the tanks. The remaining organism were segregated in stainless steel wirecloth basket (5.5 cm diameter x 7.5 cm depth) suspended around the circumference of the vessel (baskets raised and lowered in the water column at 1 rpm). Total biological loading (all species combined) was 0.5 g/l test medium. The water temperature during the test was 20 degrees, with a 16 hr photoperiod. Each test was performed twice.

**TEST ORGANISMS**

The first and second larval instar of the water flea (daphnia magna, 10 per exposure concentration) was used in this investigation. The organisms were acclimated to control diluent water in breeding/rearing tanks, and food withheld for 24 hr preceding the test.

**PHYS-CHEM PARAMETERS**

Water temperature, dissolved oxygen and pH were recorded daily (but not reported).

**BIOLOGICAL OBSERVATIONS**

Survival and behavior were recorded daily. Dead daphnia were removed when observed. All species were exposed for 96 hr. If during the test more than 5/10 of any one species of test species were found dead, additional aquaria containing lower concentrations of test solution were set up.

**DETERMINATION OF LC50**

LC50 values were calculated (computer model) based upon the log exposure concentration and the angle transformed percent mortality.

**Result:** Trial 1 LC50 = 0.25 mg/l

Trial 2 LC50 = 0.40 mg/l

**Test substance:** (Results presented in tabular form, no further information)  
Described as allyl alcohol; no further information available.  
**Conclusion:** Under the conditions of this study (static conditions), the 96 hr EC50 for allyl alcohol in the water flea (Daphnia magna) was in the range 0.25-0.40 mg/l.

**Reliability:** (2) valid with restrictions  
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

22-OCT-2003

(10)

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

**Remark:** NO DATA LOCATED  
22-OCT-2003

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

**4.5 Chronic Toxicity to Aquatic Organisms**

**4.5.1 Chronic Toxicity to Fish**

**4.5.2 Chronic Toxicity to Aquatic Invertebrates**

**TERRESTRIAL ORGANISMS**

**4.6.1 Toxicity to Sediment Dwelling Organisms**

**4.6.2 Toxicity to Terrestrial Plants**

**4.6.3 Toxicity to Soil Dwelling Organisms**

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

**4.7 Biological Effects Monitoring**

**4.8 Biotransformation and Kinetics**

**4.9 Additional Remarks**

### 5.0 Toxicokinetics, Metabolism and Distribution

In Vitro/in vivo: In vivo  
Type: Metabolism  
Species: rat

Year: 1972  
GLP: no  
Test substance: as prescribed by 1.1 - 1.4

Method: ANIMALS AND TREATMENTS  
Male SD rats (200g) were pretreated with either saline (0.5 ml i.p.) or pyrazole (375 mg/kg bwt i.p.; inhibitor of hepatic alcohol dehydrogenase) 2 hr prior to administration of allyl alcohol (0.05 ml/kg bwt i.p.; 2.46 mCi/mmmole).

Comment: Assuming a density of 0.85, this regime was equivalent to approx. 42.5 mg allyl alcohol/kg bwt.

#### AUTORADIOGRAPHY

Paraffin sections from liver, lung and kidney were coated with Kodak NTB-2 emulsion, developed for 4 wk and later stained with hemotoxylin and eosin. Comment: since no steps were taken to prevent extraction of unbound radiolabel from the tissue into the organic solvents used to embed the tissues, the author assumed that most of the exposed grains of the emulsion were indicative of label covalently bound to tissue sections.

#### COVALENT BINDING

Animals were sacrificed 6, 8 or 24 hr post-treatment with allyl alcohol. Samples of liver, lung and kidney were homogenized in 4 volumes of water, and protein/nucleic acid precipitated with an equal volume ice cold 20% trichloroacetic acid. The precipitate was extracted 5 times with 10 ml methanol (60 degrees C) to remove radioactivity (further extractions ineffective at removing any additional label). The pellet was dissolved in NaOH (1.0 N) and aliquots taken for liquid scintillation counting.

Result: Photomicrographs included in the publication show that extensive periportal necrosis was present 24 hr after administration of allyl alcohol, whereas no microscopic changes were visible in lungs or kidney (photomicrographs not presented).

Covalent binding studies demonstrated a time-dependent decrease in amount of label bound in liver, whereas little radioactivity was present in lung and kidney. Autoradiograms (included in report) demonstrated that most of the binding occurred in the periportal zone, with little present in the centrilobular region.

Inhibition of alcohol dehydrogenase fully prevented hepatic

necrosis, and decreased the amount of label bound to liver by approx. 80%. Autoradiograms confirmed that binding of <sup>14</sup>C-allyl alcohol was markedly reduced in periportal hepatocytes. Covalent binding in lung was also decreased by pretreatment with pyrazole, whereas renal binding was unaffected.

## Covalent binding data:

Treatment (n)	Time (hr)	pmol <sup>14</sup> C-allyl alcohol/mg protein		
		Liver	Lung	Kidney
Control (5)	8	119.5	16.1	10.7
Pyrazole (2)	8	21.6*	11.2	4.2
Control (2)	24	80.2	10.5	3.6
Pyrazole (2)	24	12.9*	4.9*	2.4

\* P<0.05, test not stated

**Test substance:** Described as <sup>14</sup>C-allyl alcohol, specific activity 2.46 mCi/mmol; no further information available.

**Conclusion:** Results from these studies indicate that both binding of <sup>14</sup>C-allyl alcohol to liver macromolecules and subsequent periportal hepatic necrosis are mediated by a metabolite of allyl alcohol. This conclusion is compatible with the hypothesis that the toxic metabolite is acrolein.

**Reliability:** (2) valid with restrictions  
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

22-OCT-2003

(32)

**In Vitro/in vivo:** In vivo  
**Type:** Metabolism  
**Species:** rat

**Year:** 1983  
**GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** ANIMALS AND TREATMENTS  
Male SD rats (200-220g; n=4) were treated (0.05 ml, i.p.) with either allyl alcohol or deuterated allyl alcohol (d<sub>2</sub>-allyl alcohol). After 24 hr, surviving animals were killed by exsanguination (blood collected in heparinised beakers) and the liver excised.

Comment: Assuming a density of 0.85, 0.05 ml is equivalent to approx. 42.5 mg/kg bwt.

ASSESSMENT OF LIVER DAMAGE  
Samples of liver were fixed (buffered formalin), paraffin sections prepared and stained with hemotoxylin and eosin.

Cellular damage was assessed by the method of Mitchell et al. (1973) J Pharmacol Exp Ther, 187, 185. Glutaryl-pyruvate transferase levels (GPT) in plasma were determined by a external laboratory (Pathologists Central Laboratory, Seattle).

#### COVALENT BINDING

The extent of covalent binding was determined in rats given 0.05 ml (i.p.) 14C-allyl alcohol or d2-14C-allyl alcohol as described by Reid (1972): see preceding record.

#### IN VITRO METABOLISM

Metabolism of allyl alcohol and d2-allyl alcohol by hepatic 9000 g supernatant (+/- pyrazole; alcohol dehydrogenase inhibitor), 104,000 g cytosol (+/- disulfiram; inhibitor of aldehyde dehydrogenase) and microsomal fraction (+/- NADPH; epoxidation of allyl alcohol to glycidol) was followed using the semicarbazide reaction (formation chromophore absorbing at 257 nm). Standards containing known amounts of acrolein were run in parallel.

**Result:** Hepatic necrosis (score: 1.75) and plasma GPT levels (2540 mU/ml) were 7-8 fold greater at 24 hr post-treatment in rats given allyl alcohol compared to rats given an equivalent dose of d2-allyl alcohol (necrosis score: 0.25; GPT 341 mU/ml).

Covalent binding 8 hr post-treatment with 14C-allyl alcohol was 155 pmol/mg protein compared with 48 pmol/mg protein in animals given d2-14C-allyl alcohol (3 fold difference).

NADH-dependent formation of acrolein and acrylic acid was 51-96% greater when allyl alcohol was used as substrate compared to when d2-allyl alcohol was present:

	Acrolein nmol/min/mg protein			
	AA	d2-AA	AA	d2-AA
None	0.0	0.0	0.0	0.0
NADH	48.0	31.2***	46.2	30.5***
NADH/pyrazole	16.6	11.1**	14.8	10.2**

	Acrylic acid nmol/min/mg protein			
	AA	d2-AA	AA	d2-AA
None	0.0	0.0	0.0	0.0
NADH	5.0	3.1***	5.5	2.8***
NADH/pyrazole	1.8	0.0***	1.7	0.0***

\*\* P<0.01; \*\*\* P<0.001 (test not stated)

There was no difference in the rate of appearance or disappearance of glycidol during microsomal incubation with allyl alcohol or d2-allyl alcohol.

**Test substance:** Deuterated (d2) allyl alcohol was prepared by custom synthesis and purified by preparative gas chromatography (>99.5% pure).

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<sup>14</sup>C-allyl alcohol was purchased from ICN Chemical and Radioisotope Division (Irvine, CA) with a specific activity of 10.8 mCi/mmol.

**Conclusion:** Deuterated <sup>14</sup>C-allyl alcohol (0.75 mCi/mmol) was prepared by micro custom synthesis from 1-<sup>14</sup>C-acrylic acid. Rats given a single i.p. treatment of allyl alcohol exhibited greater hepatic necrosis, elevated levels of plasma GPT and greater covalent binding to liver protein than rats given an equivalent dose of deuterated allyl alcohol. These differences correlated with significantly greater formation of acrolein and acrylic acid by liver fractions in vitro when allyl alcohol was substrate compared to that seen with deuterated allyl alcohol. These NADH-dependent reactions were sensitive to inhibition by pyrazole and disulfiram, indicating a role for alcohol- and aldehyde dehydrogenases in the hepatic metabolism of allyl alcohol.

**Reliability:** (2) valid with restrictions  
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

31-OCT-2003

(30)

### 5.1 Acute Toxicity

### 5.1.1 Acute Oral Toxicity

**Type:** LD50  
**Species:** rat  
**Strain:** Osborne-Mendel  
**Sex:** male/female  
**No. of Animals:** 10  
**Vehicle:** water  
**Value:** = 70 mg/kg bw

**Year:** 1964  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** Groups of young Osborne-Mendel rats (5 per sex per dose level) were fasted (18 hr) prior to administration of 2% aqueous allyl alcohol by gavage (dose range or number of treatment groups not stated). Animals were observed for up to 2 weeks. The LD50 was calculated according to the method of Litchfield and Wilcoxon (1949) J Pharmacol 96, 99.

**Result:** LD50 = 70 mg/kg bw (95% CI=63-79).  
  
Clinical signs: depression, colorless secretion from eyes, diarrhea, unkempt appearance.  
  
Onset of death: between 4 hr and 4 d.

**Test substance:** Described as allyl alcohol; no further information available.  
**Conclusion:** Under the conditions of the test, an oral LD50 of 70 mg/kg bw was obtained in male rats given allyl alcohol by oral gavage.  
**Reliability:** (2) valid with restrictions  
Study available for review. Early investigation, briefly reported methods and findings but considered suitable for assessment.

15-NOV-2003

(19)

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**Type:** LD50  
**Species:** rat  
**Strain:** Long-Evans  
**Sex:** male  
**No. of Animals:** 5  
**Vehicle:** water  
**Doses:** 75-130 mg/kg bw; 79-140 mg/kg bw  
**Value:** = 99 - 105 mg/kg bw

**Year:** 1958  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** Graded amounts of a 1% solution of allyl alcohol were administered by gavage (dosing needle) to groups of 5 male rats (body weights: 111-143 g or 170-252 g; two studies). Surviving animals were observed for up to 10 days.

No further experimental details provided.

The LD50 was calculated according to the method of Weil (1952) Biometrics, 8, 343.

**Result:** The main clinical sign was described as apathy, along with anxiety. Coma and diarrhea preceded death in moribund animals.

Gross post mortem findings in decedent animals included:

- edema and congestion of the lungs
- visceral congestion
- presence of mucus in the intestinal tract
- discolored liver (some necrosis)
- swollen, discolored kidneys

Histopathological examination of tissue from decedent animals revealed:

- lung congestion
- liver damage (congestion and necrosis of periportal sinusoids, central pallor and necrosis)
- presence of heme casts and cloudy swelling in the kidney.

Similar (but less frequent) lesions were present in animals that survived the 10 d observation period.

Calculated oral LD50 values of 99 mg/kg bw (for animals weighing 170-252 g) and 105 mg/kg bw (for animals weighing 111-143 g) were obtained from the study.

**Test substance:** Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.

**Conclusion:** Under the conditions of the test, an oral LD50 of 99-105 mg/kg bw was obtained in male rats given allyl alcohol by oral gavage.

**Reliability:** (2) valid with restrictions  
Study available for review. Early investigation, briefly reported methods and findings but considered suitable for assessment.

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**Type:** LD50  
**Species:** rat  
**Strain:** Sherman  
**Sex:** no data  
**Value:** = 64 mg/kg bw

**Year:** 1948  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Remark:** No information on methods or findings available.  
**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (4) not assignable  
Study available for review. Pre-guideline, non-GLP study investigation. Only limited information available but supports overall hazard assessment.

06-OCT-2003

(37)

**Type:** LD50  
**Species:** mouse  
**Strain:** Swiss Webster  
**Sex:** male  
**No. of Animals:** 6  
**Vehicle:** water  
**Doses:** 84-110 mg/kg bw  
**Value:** = 96 mg/kg bw

**Year:** 1958  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** Graded amounts of a 1% solution of allyl alcohol were administered by gavage (dosing needle) to groups of 6 male mice (17.5-22.5 g). Surviving animals were observed for up to 10 days.

No further experimental details provided.

The LD50 was calculated according to the method of Weil (1952) Biometrics, 8, 343.

**Result:** The main clinical sign was described as apathy preceded by excitability. Ataxia was occasionally present.

Gross post mortem findings in decedent animals included:  
- occasional edema and congestion of the lungs  
- no other abnormalities present

No microscopic changes were detected.

**Test substance:** The calculated oral LD50 was 96 mg/kg bw. Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.  
**Conclusion:** Under the conditions of the test, an oral LD50 of 96 mg/kg bw was obtained in male mice given allyl alcohol by oral gavage.

**Reliability:** (2) valid with restrictions  
Study available for review. Early investigation, briefly reported methods and findings but considered suitable for assessment.

25-SEP-2003

(8)

### 5.1.2 Acute Inhalation Toxicity

**Type:** LC50  
**Species:** rat  
**Strain:** Long-Evans  
**Sex:** male  
**No. of Animals:** 6  
**Doses:** 127-225 ppm (nominal)  
**Exposure time:** 4 hour(s)  
**Value:** = 125 - 140 ppm

**Year:** 1958  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** Groups of 6 male rats (100-200 g) were exposed for 1, 4 or 8 hr to 40-2300 ppm+ allyl alcohol vapor in a glass chamber (nominal volume 19.5 l). Animals were observed for 10 days post-treatment.  
[+ equivalent to 95-5450 mg/m<sup>3</sup>; based upon 1 ppm = 2.37 mg/m<sup>3</sup>; Bevan (2001), Patty's Toxicology, 5th edition, p463]

The test atmosphere was generated by passing liquid allyl alcohol via a syringe pump into an evaporation chamber through which air flowed at 8.6 to 12.9 l/min, depending on the desired exposure concentration. The atmosphere within the chamber was allowed to equilibrate to 95-99% of the desired concentration before introduction of the animals. The nominal concentration in the chamber was calculated according to Jacobs (1949) The Analytical Chemistry of Industrial Poisons, Hazards and Solvents, 2nd edition, Interscience Publishers Inc., NY.

Glass bottles of 1 l capacity containing distilled water were connected to the sampling port of the chamber and vapor drawn through the water by suction. 0.01N bromine in acetic acid and a mercuric acetate catalyst were added to the sample, the excess bromine reduced to by iodide and the iodide titrated with 0.01N thiosulfate (Reid and Beddard (1954) Analyst, 79, 456)

The LC50 was calculated according to the method of Weil (1952) Biometrics, 8, 343.

**Result:** Coma and diarrhea preceded death in moribund animals.

Gross post mortem findings in decedent animals included:  
- edema and congestion of the lungs

- visceral congestion
- presence of mucus in the intestinal tract
- discolored liver (some necrosis)
- swollen, discolored kidneys

Histopathological examination of tissue from decedent animals revealed:

- lung congestion
  - liver damage (congestion and necrosis of periportal sinusoids, central pallor and necrosis)
  - presence of heme casts and cloudy swelling in the kidney.
- Similar (but less frequent) lesions were present in animals that survived the 10 d observation period.

A calculated 4 hr LC50 value of 165 ppm (nominal) was obtained from the study.

Chemical analysis of vapor drawn from the exposure chamber revealed a 15-25% loss of allyl alcohol. After correction therefore, the LC50 was in a range 125-140 ppm.

**Test substance:** Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.

**Conclusion:** Under the conditions of the test, an acute LC50 of 125-140 ppm (295-330 mg/m<sup>3</sup>) was obtained for male rats exposed to allyl alcohol vapor by inhalation for 4 hr.

**Reliability:** (2) valid with restrictions  
Study available for review. Early investigation, briefly reported methods and findings but considered suitable for assessment.

22-OCT-2003

(8)

**Type:** LC50  
**Species:** rat  
**Strain:** Sherman  
**Sex:** male/female  
**No. of Animals:** 6  
**Exposure time:** 4 hour(s)  
**Value:** ca. 250 ppm

**Year:** 1949  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** Six male or female Sherman rats (approx. 100 - 150 g) were exposed to allyl alcohol vapor (nominal concentrations up to 250 ppm) for 4 hr, and the animals observed for a 14 d.

The test atmosphere was generated by passing liquid allyl alcohol into an heated evaporation chamber through which metered air was forced. Rats were exposed in a 9 l desiccator fitted with inlet and outlet ports.

The reported values are nominal (based on weight of material evaporated) and not verified analytically.

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**Result:** Tabulated summary information included in the report notes that exposure to 250 ppm allyl alcohol resulted in mortality in 2/6, 3/6 or 4/6 rats.

**Test substance:** Described as allyl alcohol; no further information available.

**Conclusion:** Under the conditions of the test, an acute LC50 of 250 ppm (590 mg/m<sup>3</sup>) was obtained for male rats exposed to allyl alcohol vapor by inhalation for 4 hr.

**Reliability:** (4) not assignable  
Study available for review. Pre-guideline, non-GLP study investigation. Only limited information available but supports overall hazard assessment.

15-NOV-2003 (7)

**Type:** LC0

**Year:** 1932

**GLP:** no

**Test substance:** as prescribed by 1.1 - 1.4

**Remark:** Three groups of white rats (sex, strain not specified) were exposed to 50 ppm (n=5), 200 ppm (n=4) or 1000 ppm (n=6) allyl alcohol vapor for 7 hr/d until death.

All animals from the 1000 ppm exposure group died within 3 hr of the start of the first exposure, with signs of discomfort and labored breathing with discharge from the nose and mouth. Gross necropsy revealed hemorrhage of the lungs and, to a lesser extent, the intestinal tract, kidneys and bladder.

An unspecified number of animals died following a single exposure to 200 ppm allyl alcohol, with similar clinical symptoms to those described above.

At 50 ppm, all animals survived a 7 hr exposure.

**Test substance:** Described as allyl alcohol; no further information available.

**Conclusion:** Under the conditions of the test, rats survived a 7 hr exposure to 50 ppm (approx. 120 mg/m<sup>3</sup>) allyl alcohol vapor.

**Reliability:** (4) not assignable  
Study available for review. Early investigation, briefly reported methods and findings, supports hazard characterization.

15-NOV-2003 (27)

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### 5.1.3 Acute Dermal Toxicity

**Type:** LD50  
**Species:** rabbit  
**Strain:** other: albino (no further details)  
**Sex:** male  
**No. of Animals:** 3  
**Doses:** 25-200 mg/kg bw (4 treatment levels)  
**Value:** = 89 mg/kg bw

**Year:** 1958  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** 4 groups of 3 male rabbits (1.3-3.9 kg) were exposed to 40-250 mg/kg bw allyl alcohol.

Patches of rubber dam (3x3 cm) were placed over gauze (1 cm diameter) and sealed to clipped skin using rubber cement. Allyl alcohol (25-200 mg/kg bw) was injected through the dam, onto the skin surface, and the puncture site sealed (rubber cement). The body was then further wrapped with toweling and adhesive tape to protect the dressing.

Animals were observed for 10 days post-treatment.

The LD50 was calculated according to the method of Weil (1952) Biometrics, 8, 343.

**Result:** The main clinical sign was described as apathy, along with flushing of the skin. Ataxia and diarrhea preceded death in moribund animals.

Gross post mortem findings in decedent animals included:

- edema and congestion of the lungs
- visceral congestion
- presence of mucus in the intestinal tract
- discolored liver (some necrosis)
- swollen kidneys.

Histopathological examination of tissues from decedent animals revealed:

- lung congestion
- liver damage (congestion and necrosis of periportal sinusoids, central pallor and necrosis)
- heme casts and cloudy swelling in the kidney

Similar (but less frequent) histopathological lesions were present in animals that survived the 10 d observation period.

The calculated dermal LD50 was 89 mg/kg bw.

**Test substance:** Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.

**Conclusion:** Under the conditions of the test, a dermal LD50 of 89 mg/kg bw was obtained in the rabbit following 24 hr occluded exposure to allyl alcohol.

**Reliability:** (2) valid with restrictions  
Study available for review. Early investigation, briefly reported methods and findings but considered suitable for assessment.

22-OCT-2003 (8)

**Type:** LD50  
**Species:** rabbit  
**Strain:** no data  
**Sex:** no data  
**Value:** = .053 ml/kg bw

**Year:** 1948  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Remark:** No information on methods or findings available.

Based on a density of 0.85 g/ml, this is equivalent to approx. 45 mg/kg bw.

**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (4) not assignable  
Study available for review. Pre-guideline, non-GLP study. Limitations in design and reporting but supports overall hazard assessment.

22-OCT-2003 (37)

#### 5.1.4 Acute Toxicity, other Routes

### 5.2 Corrosiveness and Irritation

#### 5.2.1 Skin Irritation

**Species:** rabbit  
**Concentration:** undiluted  
**Exposure:** Occlusive  
**Exposure Time:** 24 hour(s)  
**No. of Animals:** 3  
**Result:** slightly irritating

**Method:** Draize Test  
**Year:** 1958  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** Allyl alcohol (0.5 ml) was applied to intact and abraded skin (ventral surface) of 3 male albino rabbits. (It is not stated if fur at the treatment site was clipped first.) The application site was covered with gauze under a rubber dam, fastened with adhesive tape.

**Result:** The test site was examined 24 hr post-application. Slight erythema was present at the application site (intact skin) of one animal when the patch was removed (24 hr timepoint) but this had fully resolved by 48 hr. No other reactions were noted.

**Test substance:** Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.

**Conclusion:** Under the conditions of this test, allyl alcohol was slightly irritating to rabbit skin.

**Reliability:** (2) valid with restrictions  
Study available for review. Early investigation, briefly reported methods and findings but considered suitable for assessment.

17-OCT-2003

(8)

**5.2.2 Eye Irritation**

**Species:** rabbit  
**Concentration:** undiluted  
**Dose:** .1 ml  
**Exposure Time:** 4 hour(s)  
**No. of Animals:** 6  
**Vehicle:** none  
**Result:** irritating

**Method:** Directive 84/449/EEC, B.5 "Acute toxicity (eye irritation)"  
**Year:** 1989  
**GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** Allyl alcohol (0.1 ml) was instilled in the eye (between lower eyelid and eyeball) of 3 adult Rsk:NZW rabbits, and the lids held together for approx. 1 s. The other eye served as a control. Eyes were examined and responses noted at 4, 24, 48, 72, 96 and 168 hr post-instillation. Erythema, chemosis, iritis and corneal opacity were recorded according to the method of Draize et al. (1944; J Pharmac exp Ther 82, 337) under a Philips TLE 22W/29 lamp.

In a second study conducted 6 mo later (3 additional rabbits), corneal swelling (corneal thickness) was also assessed using an ultrasonic pachometer (Ophthasonic pachometer, TEKNAR Inc, St Louis, MO) and the results expressed as the mean percentage increase for all 3 animals at 24, 48 and 72 hr.

The mean scores for erythema, chemosis and corneal opacity were calculated for all 6 rabbits at 24, 48 and 72 hr.

**Result:** Mean results at 24, 48 and 72 hr (n):

Erythema:	2.89 (6)
Chemosis:	1.23 (6)
Corneal opacity:	2.09 (6)
Corneal swelling (thickness):	76% (3)

(Individual, animal- or time specific results not reported).  
**Test substance:** Allyl alcohol, >99% pure, UCB, Brussels, Belgium.  
**Conclusion:** Under the conditions of the test, allyl alcohol was irritating to rabbit eye.  
**Reliability:** (2) valid with restrictions  
 Study available for review. Guideline study. Briefly reported methods and findings but considered suitable for assessment.

15-NOV-2003

(17)

**Species:** rabbit  
**Concentration:** undiluted  
**Dose:** .05 ml  
**Exposure Time:** 48 hour(s)  
**No. of Animals:** 3  
**Result:** irritating

**Method:** Draize Test  
**Year:** 1958  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** Allyl alcohol (0.05 ml) was instilled into the left eye of 3 male albino rabbits.

The eyes were examined after 1 hr for signs of irritation (first unstained, then after application of 5% fluorescein sodium). Further examinations were carried out at 24 hr and 48 hr and during the subsequent week.  
**Result:** Conjunctival erythema (affecting 3/3 rabbits) and edema (affecting 1/3 rabbits) was present 1 hr post-instillation (no numerical scores reported).

At 24 hr, conjunctival erythema (score 4-6; affecting 3/3 rabbits), corneal opacity (score 5-10; affecting 2/3) and injection of the iris (score 1; affecting 1/3) was noted.

48 hr post-instillation, conjunctival redness (score 2-6; affecting 3/3 rabbits) and corneal opacity (score 5; affecting 1/3) but no iridial effects were present.

All eyes appeared normal by the end of 1 week.  
**Test substance:** Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.  
**Conclusion:** Under the conditions of this test, allyl alcohol was irritating to rabbit eye producing reversible conjunctival redness, iridial injection and corneal opacity that persisted at least 48 hr post instillation.  
**Reliability:** (2) valid with restrictions  
 Study available for review. Early investigation, briefly reported methods and findings but considered suitable for assessment.

17-OCT-2003

(8)

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**Species:** rabbit  
**Result:** irritating

**Year:** 1946  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** 0.005 ml or 0.02 ml allyl alcohol was instilled into the eye of an undefined number of rabbits.

18-24 hr later, the eye was examined in strong daylight, then re-examined after staining with fluorescein.

The following grading system was used to record any injuries present:

- corneal opacity (max. score = 6)
- keratoconus (max. score = 6)
- iris effects (max. score = 2)
- necrosis (visible after fluorescein staining; max. score = 6)
- total maximum score = 20

**Result:** Descriptive information presented in the report indicates that 0.02 ml allyl alcohol resulted in a total score of 5/20, while instillation of 0.005 ml resulted in a total score of 5 or less out of 20.

**INTERPRETATION**

The volume applied to the eye in these studies (0.005-0.02 ml) is less than that recommended in Guideline 405 (0.1 ml). A more pronounced response would be anticipated after instillation of 0.1 ml, suggesting that allyl alcohol would be irritating to the eye.

**Test substance:** Described as allyl alcohol; no further information available.  
**Conclusion:** Based on the available information, allyl alcohol appears irritating to the eye of the rabbit.  
**Reliability:** (4) not assignable  
Study available for review. Pre-guideline, non-GLP study investigation. Only limited information available but supports overall hazard assessment.

25-SEP-2003 (6)

### 5.3 Sensitization

#### 5.4 Repeated Dose Toxicity

Type: Sub-chronic  
Species: rat Sex: male  
Strain: Long-Evans  
Route of administration: inhalation  
Exposure period: 12 wk  
Frequency of treatment: 7 hr/d, 5 d/wk  
Doses: 0 (air), 1, 5, 20 ppm; 0 (air), 40, 60 ppm ; 0 (air),  
100, 150 ppm  
Control Group: yes, concurrent vehicle  
NOAEL: = 20 ppm  
LOAEL: = 40 ppm

Year: 1958  
GLP: no  
Test substance: as prescribed by 1.1 - 1.4

**Method:** ANIMALS AND TREATMENTS  
Groups of male Long-Evans rats (10/treatment level) were exposed to allyl alcohol in three separate studies using the following exposure concentrations: 0, 1, 5 or 20 ppm; 0, 40 or 60 ppm; and 0, 100 or 150 ppm. Exposures lasted 7 hr/d, 5 d/wk for a total of 60 exposures (12 wk).

The animals were exposed in stainless steel chambers (200 l capacity). Airflow within the chamber was 10.9-21.1 l/min (3-6 air changes per hour), and the temperature in the exposure room was 20-25 degrees C.

The test atmosphere was generated by passing liquid allyl alcohol via a syringe pump into an evaporation chamber through which air flowed at 8.6 to 12.9 l/min, depending on the desired exposure concentration. The atmosphere within the chamber was allowed to equilibrate to 95-99% of the desired concentration before introduction of the animals. The nominal concentration in the chamber was calculated according to Jacobs (1949) The Analytical Chemistry of Industrial Poisons, Hazards and Solvents, 2nd edition, Interscience Publishers Inc., NY.

Clinical observations: daily  
Body weights: weekly  
Diet: no details  
Water: not specified

#### NECROPSY AND HISTOPATHOLOGY

At the end of the experimental period, survivors were weighed, decapitated under ether anesthesia and subject to a post-mortem examination. Livers, kidneys and lungs from all animals were weighed and preserved (10% formalin) along with samples of thyroid, heart, thymus, pancreas, spleen, adrenal gland, testis, bladder and brain collected from alternate animals (i.e. 5/10 per treatment level). All preserved tissues

were subject to microscopic evaluation.

#### STATISTICAL METHODS

Relative organ weights and percentage body weight gains were analyzed using Student's T-test.

**Remark:** Based on a conversion factor of 1 ppm = 2.37 mg/m<sup>3</sup> (Bevan (2001), Patty's Toxicology, 5th edition, p463), the following exposure concentrations can be derived:

ppm	mg/m <sup>3</sup>
1	2.4
2	4.7
5	12
20	47
40	95
60	142
100	237
150	355

**Result:** The achieved concentration of allyl alcohol within the exposure chambers for the higher exposure conditions was:  
40.7 +/- 3.2 ppm (24)  
61.1 +/- 2.4 ppm (24)  
103.2 +/- 8.7 ppm (22)  
166.7 +/- 17.7 ppm (14)  
Values given as mean +/-SD, number of determinations in parenthesis.

#### MORTALITY AND CLINICAL SIGNS

Four rats from the 150 ppm group died during the first exposure, 2 were dead by the following morning and 2 died during the second exposure. The remaining 2 rats from the 150 ppm group died by the 10th exposure (end of week 2). There were 6 deaths in animals exposed to 100 ppm (time period inadequately characterized), and 1 death following 4 exposures to 60 ppm allyl alcohol.

Clinical signs in the 150 ppm group included gasping, severe depression, nasal discharge, eye irritation and corneal opacity. Similar but less intense clinical signs were present in animals exposed to 40-100 ppm. No clinical signs were present in animals exposed to 20 ppm and below.

#### BODY WEIGHT

Mean percentage body weight gain was statistically significantly lower in animals exposed to 20 ppm or above:

0 ppm	134%
1 ppm	133%
5 ppm	126%
20 ppm	110% (P<0.05)

0 ppm	128%
40 ppm	90% (P<0.05)
60 ppm	75% (P<0.05)

0 ppm 135%  
100 ppm 75% (P<0.05)  
150 ppm (no survivors at 15 wk)

## RELATIVE ORGAN WEIGHTS

Relative kidney weight (g/100 g bw) was increased 8-10% in animals exposed to 40 ppm or 60 ppm allyl alcohol vapor for 12 wk:

0 ppm 0.724  
1 ppm 0.706  
5 ppm 0.765  
20 ppm 0.715

0 ppm 0.582  
40 ppm 0.629  
60 ppm 0.643 (P<0.05)

Relative lung weight (g/100 g bw) was increased after exposure to 40 ppm allyl alcohol vapor for 12 wk:

0 ppm 0.410  
40 ppm 0.435 (P<0.05)  
60 ppm 0.531 (P<0.05)

(No data given for lower exposures)

Relative liver weights for treated animals were indistinguishable from those of the controls.

## NECROPSY, HISTOPATHOLOGY

Livers from rats exposed to 150 ppm allyl alcohol appeared hemorrhagic and the lungs pale and spotted. The kidneys appeared normal. The only microscopic observation was slight congestion of the lungs and liver (no further details).

Lesions and microscopic findings at 100, 60 and 40 ppm were described as similar but less intense to those reported at 150 ppm.

There were no unusual gross or microscopic findings at 20 ppm or below.

## DERIVATION OF NOAEC

Although only limited data are available from this study, increases in relative kidney and lung weight are consistent with a LOAEC of 40 ppm. No lung data are available for animals exposed to lower concentrations, however relative kidney weights were unaffected indicating a NOAEC of 20 ppm. The NOAEC for decreased bw gain was 5 ppm.

**Test substance:** Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.

**Conclusion:** Under the conditions of this study, a sub-chronic inhalation NOAEC of 5 ppm (12 mg/m<sup>3</sup>) was obtained for decreased body weight gain in rats exposed to allyl alcohol over 12 wk. With regard to organ effects, increases in relative kidney weight were consistent with a systemic NOAEC of 20 ppm (47 mg/m<sup>3</sup>).

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**Reliability:** (2) valid with restrictions  
Study available for review. Pre-guideline, non-GLP study.  
Limitations in design and reporting but supports overall  
hazard assessment.

15-NOV-2003 (8)

**Type:** Sub-acute  
**Species:** rat **Sex:** no data  
**Strain:** no data  
**Route of administration:** inhalation

**Year:** 1932  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Remark:** Three groups of white rats (sex, strain not specified) were  
exposed to 50 ppm (n=5), 200 ppm (n=4) or 1000 ppm (n=6) allyl  
alcohol vapor for 7 hr/d until death.

All animals from the 1000 ppm exposure group died within 3 hr  
of the start of the first exposure, with signs of discomfort  
and labored breathing with discharge from the nose and mouth.  
Gross necropsy revealed hemorrhage of the lungs and, to a  
lesser extent, the intestinal tract, kidneys and bladder.

All animals exposed to 200 ppm allyl alcohol died following  
one or two exposures with similar clinical symptoms to those  
described above.

Rats exposed to 50 ppm allyl alcohol vapor survived an average  
of 30 d (no further details).

**Test substance:** Described as allyl alcohol; no further information available.  
**Reliability:** (4) not assignable  
Study available for review. Early investigation, briefly  
reported methods and findings, supports hazard  
characterization.

15-NOV-2003 (27)

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**Type:** Sub-chronic  
**Species:** rat **Sex:** male/female  
**Strain:** Wistar  
**Route of administration:** drinking water  
**Exposure period:** 15 wk  
**Frequency of treatment:** daily  
**Post exposure period:** none  
**Doses:** 0, 50, 100, 200 or 800 ppm  
**Control Group:** yes, concurrent vehicle  
**NOAEL:** = 50 ppm

**Year:** 1978  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:**

## ANIMALS AND TREATMENTS

Groups of Wistar rats (15/sex/treatment level) were exposed to allyl alcohol in the drinking water at 0 (control), 50, 100, 200 or 800 ppm for 15 weeks. Additional groups of 5 rats/sex were given 0, 200 or 800 ppm allyl alcohol for 2 wk or 6 wk. (Comment: group sizes inconsistent with OECD TG 408)

Animal supplier: commercial supplier (not specified), SPF colony.

Housing: 5/cage; 20+/-1 degree C; 50-60% relative humidity.

Body weights: recorded pre-treatment and on days 1,6,8,13,15 or 20.

Food and water intake: measured over the 24-h period preceding each weighing.

Diet: Spratts Laboratory Diet No 1, ad libitum

Water: not specified

## RENAL FUNCTION AND URINE ANALYSIS

Renal function was investigated during wk 2 or wk 5 (n=5/sex) and in wk 15 (n=12/sex). Concentrating ability (specific gravity, volume) was determined by measuring the urine volume produced during 0-6 hr of water deprivation; at wk 5 and 15, the concentration test was extended to include samples collected over 4 hr following a 16 hr period without water. Diluting ability was then assessed over 2 hr following a water load of 25 ml/kg bwt; these samples were also assessed for specific gravity, appearance and microscopic constituents (cells) as well as a semi-quantitative evaluation of glucose, ketones, bile salts and blood. At wk 5 and 15, and studies performed after 2 wk treatment, concentrating ability was determined over 2 hr following a 6 hr deprivation period.

## HEMATOLOGY

Blood collected at necropsy was assessed for hemoglobin content, packed cell volume and red cell and total leukocyte counts. A differential leukocyte count and a reticulocyte count was performed on samples from control and high dose animals. (Comment: several omissions compared with OECD TG 408.)

## CLINICAL CHEMISTRY

Serum was analyzed for urea, glucose, total protein and albumin, together with ASAT, ALAT and lactic dehydrogenase activity. (Comment: several omissions compared with OECD TG 408.)

## NECROPSY AND HISTOPATHOLOGY

At the end of the appropriate treatment period, animals were killed by exsanguination under barbiturate anesthesia following an overnight fast. Animals were subject to a post-mortem examination and any external or internal macroscopic abnormalities noted. A representative range of tissues was weighed, sampled and preserved for histopathological evaluation. (Comment: range of tissues comparable to OECD TG 408, but with some exclusions notably aorta, trachea/lungs, skin, eye, peripheral nerve, bone marrow).

## STATISTICAL METHODS

Mean body weights, food and water intake and organ weights were analyzed using Student's t-test. Renal function data were analyzed by the method of White (1952; Biometrics, 8, 33).

**Result:**

## INTAKE OF TEST SUBSTANCE

The calculated mean intake of allyl alcohol over the course of the study (based on body weight and water intake data) was:

Males: 0, 4.8, 8.3, 14.0, 48.2 mg/kg bw/d

Females: 0, 6.2, 6.9, 17.1 and 58.4 mg/kg bw/d

## BODY WEIGHT, FOOD INTAKE AND WATER CONSUMPTION

Body weight was significantly decreased in males given 100 or 200 ppm allyl alcohol from wk 2 of treatment, and from males and females given 800 ppm following a single day's treatment. Terminal body weights (g) at week 15 were:

- Males

Control: 472

50 ppm: 453

100 ppm 449 (ns)

200 ppm: 420 (P<0.01)

800 ppm: 270 (P<0.001)

- Females

Control: 253

50 ppm: 260

100 ppm 260

200 ppm: 257

800 ppm: 205 (P<0.001)

Food intake was significantly decreased in male rats from the 200 (-11%; P<0.01) and 800 ppm (-32%; P,0.001) groups, and in high dose females (-18%; P,0.001).

There was a statistically significant decrease in water intake in all treated groups:

- Males

Control: 27.7

50 ppm: 24.2 (P<0.01)  
100 ppm 19.4 (P<0.01)  
200 ppm: 15.5 (P<0.001)  
800 ppm: 10.0 (P<0.001)

- Females

Control: 26.5  
50 ppm: 22.0 (P<0.05)  
100 ppm 17.2 (P<0.001)  
200 ppm: 14.4 (P<0.001)  
800 ppm: 9.8 (P<0.001)

HEMATOLOGY AND CLINICAL CHEMISTRY

No abnormalities reported. (Comment: data not available for evaluation.)

RENAL FUNCTION AND URINE ANALYSIS

There was a statistically significant decrease (-50% to -75%) in excretion of cells in male rats following 2, 5 and 15 wk treatment with 800 ppm allyl alcohol.

Urine concentrating ability (ml/6 hr) was significantly impaired in a time- and dose dependent manner in males:

- Wk 2

Control: 1.9  
200 ppm: 2.2  
800 ppm: 0.6 (P<0.05)

- Wk 5

Control: 3.8  
200 ppm: 0.9 (P<0.01)  
800 ppm: 0.9 (P<0.01)

- Wk 15

Control: 4.5  
50 ppm: 2.7  
100 ppm: 2.4 (P<0.01)  
200 ppm: 1.8 (P<0.001)  
800 ppm: 0.8 (P<0.05)

Essentially similar, but statistically non-significant, changes were present in females.

Urine concentrating ability over 16-20 hr was unaffected by treatment with allyl alcohol.

Urine volume (ml) was statistically significantly decreased during the dilution test at wk 2, 5 and 15 for animals (both sexes) treated with allyl alcohol in drinking water at 200 ppm or above. Representative data for males:

- Wk 2

Control: 4.3  
200 ppm: 0.7 (P<0.01)  
800 ppm: 0.3 (P<0.01)

- Wk 5

Control: 7.3  
200 ppm: 2.2 (P<0.05)  
800 ppm: 0.9 (P<0.05)

- Wk 15  
Control: 8.4  
50 ppm: 7.5  
100 ppm: 5.9  
200 ppm: 3.6 (ns)  
800 ppm: 0.5 (P<0.001)

Specific gravity was increased (approx. 1-4%) during the dilution test at wk 2, 5 and 15 for males and females given allyl alcohol in drinking water at 200 ppm or above. These changes were generally statistically significant.

#### POST MORTEM EXAMINATION

No gross abnormalities were present in any sex/treatment group.

Absolute organ weights were generally decreased in males, and to a lesser extent in females, in a time- and treatment related manner after ingestion of 100 ppm allyl alcohol or above. Although statistically significant (especially in high dose males), these decrements were consistent with the lower body weights recorded in treated animals. The exception was absolute kidney weight for females, which was statistically significantly increased (11-13%; P<0.001) at week 15 in the 100, 200 and 800 ppm treatment groups:

	--abs. kidney wt--	
	males	females
Control	2.42	1.48
50	2.43	1.48
100	2.48	1.65***
200	3.07	1.67***
800	2.10	1.64***

Relative organ weights (g/100 g bwt) were generally increased to a statistically significant extent in high dose animals of both sexes at study termination. Relative kidney weights and relative stomach weights, in contrast, were increased in a dose-dependent manner in females at week 2 and in both sexes following 6 or 15 weeks of treatment. Results at 15 wk summarized below:

	--rel. kidney wt--		--rel. stomach wt--	
	males	females	males	females
Control	0.56	0.59	0.37	0.50
50	0.55	0.60	0.39	0.50
100	0.58	0.67***	0.42***	0.54*
200	0.59**	0.70***	0.41**	0.52
800	0.73***	0.83***	0.50***	0.66***

#### HISTOPATHOLOGICAL EVALUATION

Minor changes were present in the microscopic appearance of the liver (occasional vacuolated cells, scattered individual cell necrosis with lymphocyte infiltration), kidneys (occasional vacuolated tubular cells) and spleen (mild degree

of peribronchial lymphocyte infiltration) however these occurred at a similar incidence in control and treated animals. (No microscopic changes were reported in stomach.)

## DERIVATION OF NOAEL

The majority of findings from this study, in particular lower body weights, alterations in organ weights and changes in renal function, appear secondary to a reduction in water intake that was particularly pronounced in high dose animals. This is presumed to reflect poor palatability of the dosing solutions. Against this background, there was a more generalized increase in absolute kidney weight (females), relative kidney weight (both sexes) and relative stomach weight (both sexes) in the intermediate and high dose groups after 15 wk of treatment. While local irritation (stomach) or dehydration (kidney) may have contributed in part to these findings, they may also be indicative of mild systemic renal toxicity with a sub-chronic NOAEL of 50 ppm (6.2 mg/kg bwt/d) in females and 100 ppm (8.3 mg/kg bwt/d) in males.

**Test substance:** Allyl alcohol, 99% pure, SG (20 degree C) 0.849-0.852; bpt 95-98 degrees C, supplied by Bush Boake Allen Ltd, London.

**Conclusion:** Under the conditions of this study, a sub-chronic NOAEL of 50 ppm allyl alcohol in drinking water (equivalent to 6.2 mg/kg bw/d) was obtained for female rats and 100 ppm (equivalent to 8.3 mg/kg bwt/d) was obtained for males, based upon treatment and time related increases relative kidney weight. Possible confounding by dehydration (caused by poor palatability of the test solutions) cannot, however, be completely excluded.

**Reliability:** (2) valid with restrictions  
Study available for review. Pre-guideline, non-GLP study. Reasonably well reported methods and results, suitable for assessment.

21-NOV-2003

(5)

**Type:** Sub-chronic  
**Species:** rat **Sex:** male/female  
**Strain:** Long-Evans  
**Route of administration:** drinking water  
**Exposure period:** 13 wk  
**Frequency of treatment:** continuous  
**Doses:** 0 (water), 1, 5, 50, 100 or 250 ppm; 0, 500 or 1000 ppm  
**Control Group:** yes, concurrent vehicle  
**NOAEL:** = 100 ppm  
**LOAEL:** = 250 ppm

**Year:** 1958  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** ANIMALS AND TREATMENTS  
Groups of male and female Long-Evans rats (10/sex/treatment level) were exposed to allyl alcohol in drinking water in two separate studies using the following exposure concentrations: 0, 1, 5, 50, 100 or 250 ppm; 0, 500 or 1000 ppm. Treatment was

continuous and lasted for 13 wk.

Stock solutions were prepared weekly in brown glass bottles with plastic stoppers.

Clinical observations: daily  
Body weight: weekly  
Water consumption: weekly  
Diet: no details

#### NECROPSY AND HISTOPATHOLOGY

At the end of the experimental period, survivors were weighed, decapitated under ether anesthesia and subject to a post-mortem examination. Livers and kidneys from all animals were weighed and preserved (10% formalin). Samples of duodenum, thyroid, heart, thymus, pancreas, spleen, adrenal gland, testis, ovary, bladder and brain collected from alternate animals (i.e. 5/10 per treatment level). All preserved tissues were subject to microscopic evaluation.

#### STATISTICAL METHODS

Relative organ weights and percentage body weight gains were analyzed using Student's T-test.

#### Result:

#### WATER CONSUMPTION AND INTAKE OF TEST SUBSTANCE

Water consumption decreased in a treatment-related manner in both sexes:

	--ml/rat/day--	
	males	females
0 ppm	145	177
1 ppm	131	170
5 ppm	124	188
50 ppm	118	147
100 ppm	116	133
250 ppm	102	135
0 ppm	151	172
500 ppm	82	87
1000 ppm	72	67

Calculated intake of allyl alcohol was as follows:

	--mg/kg bw/d--	
	males	females
0 ppm		
1 ppm	0.13	0.17
5 ppm	0.62	0.94
50 ppm	5.9	7.3
100 ppm	11.6	13.2
250 ppm	25.5	34.0
0 ppm		
500 ppm	41.0	43.7
1000 ppm	72.0	67.4

#### CLINICAL SIGNS

Occasional crusting or swelling of the eyelids was the only clinical sign observed (no detail of any dose/severity relationship).

Two males from the 250 ppm treatment group lost weight; one was sacrificed after 5 wk, the other died during week 10. Pulmonary edema was observed in one animal at post-mortem with necrosis of the intestinal mucosa in the other; liver and kidney were normal.

#### NECROPSY OBSERVATIONS

Few abnormalities were noted at necropsy at week 13:

- perirenal fat was decreased in the 500 ppm group and absent at 1000 ppm
- the livers from two high dose females were pale with a soft, spongy yellowish appearance with well organized areas of necrosis with regeneration observed upon microscopic examination (appearance and distribution considered consistent with infarction by the study authors)
- perivascular cuffing present in brain from one high dose female
- the authors state there were no other findings of interest

#### BODY WEIGHT

Mean percentage body weight gain was statistically significantly lower in animals exposed to 500 ppm allyl alcohol in drinking water and above:

	males	females
0 ppm	76	51
1 ppm	79	56
5 ppm	98	51
50 ppm	108	60
100 ppm	92	47
250 ppm	106	42
0 ppm	229	139
500 ppm	99*	70*
1000 ppm	51*	43*

\* = P<0.05

#### RELATIVE ORGAN WEIGHTS

Relative kidney weight (g/100 g bw) was increased in a dose related manner following 13 wk treatment with allyl alcohol in drinking water:

	males	females
0 ppm	0.817	0.776
1 ppm	0.792	0.759
5 ppm	0.816	0.766
50 ppm	0.842	0.767
100 ppm	0.829	0.794
250 ppm	0.826*	0.882*
0 ppm	0.610	0.612
500 ppm	0.760*	0.778*

1000 ppm 0.815\* 0.834\*  
\* = P<0.05

Relative liver weight (g/100 g bw) was increased 11-22% in males given allyl alcohol in drinking water at 250 ppm or above for 13 wk; less consistent increases present in females:

	males	females
0 ppm	3.02	3.59
1 ppm	2.91	3.60
5 ppm	3.01	3.62
50 ppm	3.03	3.72
100 ppm	3.32+	3.30
250 ppm	3.35*	3.46

0 ppm	3.03	3.26
500 ppm	3.50	3.66
1000 ppm	3.69*	3.41

\* = P<0.05

(+ Note: value reported as 0.332; presumed type-setting error)

#### DERIVATION OF NOAEL

Although only limited data are available from this study, statistically significant increases in relative kidney weight in rats of both sexes given 250 ppm or above allyl alcohol in drinking water, with a concurrent decrease in body weight gain (significant at 500 ppm and 1000 ppm), appears indicative of toxicity. Relative liver weights were also increased in male rats given 250 ppm and above, although this change was not always statistically significant. These observations point to a NOAEL of 100 ppm (equivalent to 11.6-13.2 mg/kg bw/d in males and females, respectively).

**Test substance:** Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.

**Conclusion:** Under the conditions of this study, a sub-chronic oral NOAEL of 100 ppm allyl alcohol in drinking water (equivalent to 11.6-13.2 mg/kg bw/d) was obtained for the rat, based upon treatment related increases in relative kidney and liver weights at higher exposures.

**Reliability:** (2) valid with restrictions  
Study available for review. Pre-guideline, non-GLP study. Limitations in design and reporting but supports overall hazard assessment.

25-NOV-2003

(8)

**Type:** Sub-chronic  
**Species:** rat **Sex:** male/female  
**Strain:** Fischer 344  
**Route of administration:** gavage  
**Exposure period:** 13 wk  
**Doses:** 0, 1.5, 3, 6, 12 or 25 mg/kg bwt/d

**GLP:** yes  
**Test substance:** other TS

**Remark:** Information available from the NTP website indicated that the sub-chronic toxicity of allyl alcohol has been investigated in F-344 rats following gavage administration (NTP study No. C93009). No published report is currently available. This information is included in this set of Robust Summaries for completeness.

25-NOV-2003

(29)

**Type:** Sub-chronic  
**Species:** mouse **Sex:** male/female  
**Strain:** B6C3F1  
**Route of administration:** gavage  
**Exposure period:** 13 wk  
**Doses:** 0, 3, 6, 12, 25 or 50 mg/kg bwt/d

**GLP:** yes  
**Test substance:** as prescribed by 1.1 - 1.4

**Remark:** Information available from the NTP website indicated that the sub-chronic toxicity of allyl alcohol has been investigated in B6C3F1 mice following gavage administration (NTP study No. C93009). No published report is currently available. This information is included in this set of Robust Summaries for completeness.

25-NOV-2003

(29)

### 5.5 Genetic Toxicity 'in Vitro'

**Type:** Bacterial reverse mutation assay  
**System of testing:** Salmonella typhimurium TA1535, TA1537, TA1538, TA98 and TA100  
**Concentration:** 10-500 ug/plate  
**Cytotoxic Concentration:** 500 ug/plate  
**Metabolic activation:** with and without  
**Result:** positive

**Year:** 1980  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** Tester strains TA1535, TA1537, TA1538, TA98 and TA100 were used with or without S9 from Arochlor 1254 treated rats or hamsters. [Comment: Hamster S9 was used whenever the test

compound was not mutagenic with rat S9.]

Testing was conducted using plate incorporation or liquid pre-incubation (45 min at 37 degrees C) methodology, with independent repeat.

Sodium azide, 9-aminoacridine, 2-nitrofluorene and 2-aminoanthracene were used as positive controls (all tester strains, with or without rat and hamster S9).

A compound was considered mutagenic if the number of revertants was twice the background, and a dose-response curve was demonstrable.

**Result:** Allyl alcohol was mutagenic only in TA1535 in the liquid pre-incubation test, with distilled water as solvent in the presence of hamster S9.

Representative results from one repeat (other not reported):

Dose (ug)	Revertants/plate	
	-S9	+S9
0 (water)	16	22
10	14	38
25	21	37
50	15	55+
75	10	62+
100	17	62+
125	15	64+
175	5	81+
200	10	71+
300	10	55+
500	T	21

+ value at least twice control mean  
T toxic

Cytotoxicity was apparent at 500 ug in the plate incorporation test but not at this concentration in the liquid preincubation test.

A satisfactory response was obtained with the positive control substances.

**Test substance:** Allyl alcohol, >95%, Aldrich Chemical Company (no further details).

**Conclusion:** Under the conditions of the test, a positive response was obtained with TA1535 in a liquid preincubation assay (negative with plate incorporation) in the presence of hamster S9 (negative in the presence of rat S9, negative in absence of S9). No mutagenic response was seen with TA1537, TA1538, TA98 or TA100.

**Reliability:** (2) valid with restrictions  
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

22-OCT-2003

(21)

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**Type:** Bacterial reverse mutation assay  
**System of testing:** Salmonella typhimurium TA100  
**Concentration:** up to 0.15 umol/2 ml incubation (equivalent to approx. 9 ug/2 ml)  
**Cytotoxic Concentration:** <50% survival at 0.075 umol/2 ml incubation (approx. 4.5 ug/2 ml)  
**Metabolic activation:** with and without  
**Result:** positive

**Year:** 1982  
**GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** Tester strain TA100 was used in a liquid pre-incubation assay (tightly closed screw-capped vials, 37 degrees C, shaking, 90 min) in the absence and presence of S9 (source not specified). An aliquot from each incubation was diluted and plated onto histidine-containing medium. Mutation frequencies were determined as the number of revertants per umol allyl alcohol. The assay was conducted with an independent repeat.

The concentration range used is not stated. Graphical data indicate that 5 concentrations up to 0.15 umol per 2 ml liquid incubation were employed. Based upon a molecular weight of 58.08, this equates to approx. 9 ug.

Sodium azide was used as positive control in the absence of S9, and 2-aminoacridine in the presence of S9.

**Remark:** The authors note that <1 ppm acrolein was present in sample of allyl alcohol used in these studies. Concurrent data on acrolein, also included in this publication, lead them to conclude that acrolein (at this concentration) would not have contributed to the mutagenic response observed.

The authors suggest that conversion of allyl alcohol to acrolein by bacterial alcohol dehydrogenase(s) may account for the strong positive response obtained.

**Result:** Graphical data demonstrate a clear inverse correlation between survival and induction of revertants in TA100 in the absence of S9.

In the absence of S9, there was a linear increase in the number of revertants per plate over a concentration range of approx. 0.04-0.15 umol/2 ml (equivalent to approx. 2-9 ug).

Survival was also decreased in the presence of S9 (weak mutagenic response), however this effect was considerably less pronounced than was seen in the presence of S9.

A mutation frequency of 750 revertants/umol (approx. 13 revertants/ug) was obtained in the absence of S9, and 145 revertants/umol (approx. 2 revertants/ug) in its presence.

**Test substance:** Allyl alcohol, 99.9% pure by GC analysis, Merck, Darmstadt, Germany

**Conclusion:** Under the conditions of the test, a positive response was obtained with TA100 in a liquid preincubation assay in absence of rat S9 (negative in the presence of S9).

**Reliability:** (2) valid with restrictions  
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

22-OCT-2003

(24)

**Type:** Bacterial reverse mutation assay  
**System of testing:** Salmonella typhimurium TA100, TA1535, TA97, TA98  
**Concentration:** 0.3-166 ug/plate or 3-333 ug/plate  
**Cytotoxic Concentration:** 333 ug/plate  
**Metabolic activation:** with and without  
**Result:** negative

**Method:** other: US-NTP standard protocol  
**Year:** 2003  
**GLP:** yes  
**Test substance:** as prescribed by 1.1 - 1.4

**Remark:** Only limited information is available for this study which was conducted in the absence or presence of 10% or 30% rat or hamster S9 using a preincubation protocol.

It was run with an independent repeat.

DMSO was the vehicle control with (currently unspecified) positive controls for each strain.

**Test substance:** Described as allyl alcohol; no further information available.

**Conclusion:** Under the conditions of the test, no mutagenic activity was detected in 4 strains of Salmonella typhimurium (including TA100 and TA1535) in the absence or presence of rat or hamster S9.

**Reliability:** (2) valid with restrictions  
GLP compliant, NTP guideline study but only limited information available for review, hence Reliability 2.

18-NOV-2003

(29)

**Type:** Bacterial reverse mutation assay  
**System of testing:** Salmonella typhimurium TA1535, TA1537, TA1538, TA98, TA100  
**Concentration:** 0.025, 0.05, 0.10 ul/plate  
**Cytotoxic Concentration:** >0.10 ul/plate  
**Metabolic activation:** with and without  
**Result:** negative

**Year:** 1981  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** SPOT TEST  
The ability of allyl alcohol (0.05 ul) to induce reversion in Salmonella typhimurium tester strains TA1535, TA1537, TA1538,

TA98, TA100 was investigated using a spot test in the absence or presence of S9 (SD rat, Arochlor 1254 induction). The authors state that the system used was suitable for testing volatile substances. Ethyl methansulfonate (5 ul/plate; TA1535), 9-aminoacridine (10 ug/plate; TA1537), 4-nitro-o-phenyldiamine (10 ug/plate; TA1538 and TA98), methyl methansulfonate (1 ul/plate; TA100) were used as positive control substances in the absence of S9. 2-aminoanthracene (1 ug/plate) was used as positive control substance for all tester strains in the presence of S9.

PLATE INCORPORATION ASSAY

Mutagenic activity was also investigated in TA1535, TA100 and TA98 using using a plate incorporation assay and 0.025, 0.05, 0.1 ul allyl alcohol/plate in the absence or presence of S9.

Comment: Concentrations in excess of 0.05 ul (= 50 nl; spot test) or 0.10 ul (= 100 nl; plate incorporation assay) were cytotoxic (no data presented).

**Result:**

SPOT TEST

The number of his<sup>+</sup> revertants per plate was highly comparable in control and test cultures for all 5 tester strains both in the absence or presence of S9. A satisfactory response was obtained with the positive control substances.

PLATE INCORPORATION ASSAY

There was no increase in revertants in any of the 3 tester strains in the absence or presence of S9.

**Test substance:**

Allyl alcohol, analytical grade, Fluka AG (no further details).

**Conclusion:**

Under the conditions of the test, allyl alcohol (highest non-toxic concentration) was not mutagenic in a spot test (5 stains of Salmonella typhimurium including TA100 and TA1535) or a plate incorporation assay (3 tester strains).

**Reliability:**

(2) valid with restrictions

Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

16-NOV-2003

(31)

**Type:** Mammalian cell gene mutation assay  
**System of testing:** V79 cells, 6-thioguanine resistance  
**Concentration:** 1 or 2 uM (equivalent to 58 or 116 ng/ml)  
**Cytotoxic Concentration:** >2 uM  
**Metabolic activation:** no data  
**Result:** positive

**Year:** 1990

**GLP:** no data

**Test substance:** as prescribed by 1.1 - 1.4

**Method:** Growing cultures of V79 cells in complete Williams medium E (WE; containing 10% fetal bovine serum) were exposed to allyl alcohol (1 uM, 2 uM) for 2 hr, transferred to fresh medium for

24 hr, harvested and then reseeded ( $10^6$  cells) into fresh medium for 10 d, with one subdivision.

These cells were harvested and divided for assessment of absolute plating efficiency (after 7 d growth in complete WE) and for mutation frequency ( $3.17 \times 10^5$  cells plated in presence of 3  $\mu\text{M}$  6-thioguanine; 10 d incubation period with one change of medium).

Incubations were performed at 37 degrees C in 95% air:5% carbon dioxide and 80% relative humidity.

No exogenous metabolic activation was included.

No statistical analysis was applied to the data.

Comment: The methods indicate that the concentration of fetal bovine serum present in the WE medium varied between 0-10% during exposure to allyl alcohol. The intention was to investigate the possible protective role of thiol groups on any mutagenic response observed.

**Result:** A mutation frequency of  $14 \pm 8$  mutants/ $10^6$  survivors was reported after exposure to 1  $\mu\text{M}$  allyl alcohol (58 ng/ml), and  $37 \pm 12$  after exposure to 2  $\mu\text{M}$  (116 ng/ml; results are mean and SD of 8 plates from a single experiment).

No concurrent control data are reported.

The thiol status of the above incubations is not reported. Other studies described in this paper indicate that the magnitude of any mutagenic response was greatly diminished by inclusion of 10% fetal bovine serum in the assay. It is therefore assumed that no fetal bovine serum was present.

The authors conclude that allyl alcohol was mutagenic in v79 cells in vitro.

**Test substance:** Allyl alcohol, Aldrich Chemical Co., Milwaukee, WI (no further details).

**Conclusion:** Under the conditions of the assay, allyl alcohol was reported to be mutagenic in V79 cells in the absence of exogenous metabolic activation.

**Reliability:** (4) not assignable  
Study available for review. Briefly reported methods and findings, insufficient for full assessment, reliability cannot be assessed.

17-OCT-2003

(36)

**Type:** Bacterial forward mutation assay  
**System of testing:** Streptomyces coelicolor, resistance to streptomycin  
**Concentration:** 2-100 ul/plate  
**Cytotoxic Concentration:** >100 ul/plate  
**Metabolic activation:** without  
**Result:** negative

**Year:** 1981  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** Forward mutation of *S. coelicolor* to streptomycin resistance was investigated in a spot test (100 ul/test) or a plate incorporation assay (2-100 ul/plate).  
  
The test medium was supplemented with 1.5 ug/ml streptomycin and approx.  $2 \times 10^7$  spores (method: Carere et al. (1978) Chem Biol Interact 22, 297-308; Carere et al. (1987) Mut Res 57, 277; no further details.)  
  
Ethyl methansulfonate (2 ul/plate) was used a positive control substance.

**Result:** Allyl alcohol was ineffective at inducing mutants in both the spot test and the plate incorporation test.  
  
An acceptable response was obtained with the positive control substance.

**Test substance:** Allyl alcohol, analytical grade, Fluka AG (no further details).

**Conclusion:** Under the conditions of the test, allyl alcohol (100 ul) did not induce forward mutations in *Streptomyces coelicolor* in a spot test or a plate incorporation assay.

**Reliability:** (2) valid with restrictions  
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

16-NOV-2003 (31)

**Type:** other: fungal point mutation  
**System of testing:** Aspergillus nidulans  
**Concentration:** 10-40 ul/plate  
**Cytotoxic Concentration:** >40 ul/plate  
**Metabolic activation:** without  
**Result:** negative

**Year:** 1981  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** The induction of point mutations in *Aspergillus nidulans* (haploid strain 35), as detected by resistance to 8-azaguanine, was investigated using a spot test (20 ul allyl alcohol/test) or a plate incorporation assay (10, 20 or 40 ul allyl alcohol/plate). (Method: Bignami et al. (1980) Chem Biol

Interact 30, 9; no further details.)

Methyl methansulfonate (1 ul/plate) was used a positive control substance.

**Result:** Allyl alcohol was ineffective at inducing mutations in both the spot test and the plate incorporation test.

An acceptable response was obtained with the positive control substance.

**Test substance:** Allyl alcohol, analytical grade, Fluka AG (no further details).

**Conclusion:** Under the conditions of the test, allyl alcohol (100 ul) did not induce point mutations in *Aspergillus nidulans* in a spot test (20 ul allyl alcohol/test) or a plate incorporation assay (up to 40 ul/plate).

**Reliability:** (2) valid with restrictions  
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

17-OCT-2003 (31)

### 5.6 Genetic Toxicity 'in Vivo'

**Type:** Cytogenetic assay

**Species:** rat **Sex:** male

**Strain:** Fischer 344

**Route of admin.:** i.p.

**Exposure period:** 72 hr

**Doses:** 0, 5, 10, 20, 40, 60 or 80 mg/kg bw

**Result:** negative

**Method:** other: US-NTP standard protocol

**Year:** 2001

**GLP:** yes

**Test substance:** as prescribed by 1.1 - 1.4

**Method:** ANIMALS AND TREATMENTS  
Male F344 rats were given allyl alcohol at 5, 10 or 20 mg/kg bw (n=5/treatment) by i.p. injection on 3 consecutive days. The control group (n=4) received physiological saline. Bone marrow was collected 24 hr after the final treatment. Two thousand polychromatic erythrocytes were examined microscopically and scored for the presence of micronuclei. No further experimental details available.

POSITIVE CONTROL SUBSTANCE  
Cyclophosphamide (7.5 mg/kg bw) was used as positive control (presumed i.p. injection on 3 consecutive days, however no details available).

STATISTICAL METHODS  
Control versus test comparisons are reported together with trend analysis, however no information on methods applied.

**Result:** There was no statistically significant difference in the number of micronuclei per 1000 PCEs in rats given allyl alcohol at 5, 10 or 20 mg/kg bw/d by i.p. injection on 3 consecutive days:  
Control 1.4 MN/1000 PCE  
5 mg/kg 2.0  
10 mg/kg 1.6  
20 mg/kg 1.4  
The trend for incidence of micronucleated NCEs was non-significant.

Animals given 40, 60 or 80 mg/kg died prior to scheduled study termination.

A satisfactory response was obtained with the positive control group (24.2 MN per 1000 PCEs; P=0.0000).

**Test substance:** Allyl alcohol, CAS No 107-18-6, aliquot no. A98432 (no further details).

**Conclusion:** Under the conditions of the study, no increase in micronucleated polychromatic erythrocytes was detected in male F344 rats given allyl alcohol at doses of up to 40 mg/kg bw/d for three consecutive days.

**Reliability:** (2) valid with restrictions  
GLP compliant, NTP guideline study but only limited information available for review, hence Reliability 2.

16-NOV-2003

(29)

**Type:** Cytogenetic assay  
**Species:** mouse **Sex:** male/female  
**Strain:** B6C3F1  
**Route of admin.:** gavage  
**Exposure period:** 13 wk  
**Doses:** 0, 3, 6, 12, 25 or 50 mg/kg bw/d  
**Result:** negative

**Method:** other: US-NTP standard protocol  
**Year:** 2001  
**GLP:** yes  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** ANIMALS AND TREATMENTS  
Male and female B6C3F1 mice (n=10/sex/dose level) were given allyl alcohol at doses of 0, 3, 6, 12, 25 or 50 mg/kg bw/d by oral gavage for 13 wk. (Comment: the control vehicle is not identified; it is not stated if treatment continued 5 d/wk or 7 d/wk). Peripheral blood was collected 24 hr after the final treatment. One thousand normochromic erythrocytes were examined microscopically and scored for the presence of micronuclei. No further experimental details available.

POSITIVE CONTROL SUBSTANCE  
No positive control substance was used.

STATISTICAL METHODS

Control versus test comparisons are reported together with trend analysis, however no information on methods applied.

**Result:** There was no statistically significant difference in the number of micronuclei per 1000 NCEs at any treatment level in either sex:

- males

Control	1.1 MN/1000 NCE
3 mg/kg	1.2
6 mg/kg	1.7
12 mg/kg	1.4
25 mg/kg	1.2
50 mg/kg	1.6

- females

Control	0.7 MN/1000 NCE
3 mg/kg	0.9
6 mg/kg	1.0
12 mg/kg	0.7
25 mg/kg	1.5
50 mg/kg	1.1

The trend for incidence of micronucleated NCEs was non-significant.

**Test substance:** Allyl alcohol, CAS No 107-18-6, aliquot no. A98432 (no further details).

**Conclusion:** Under the conditions of the study, no increase in micronucleated normochromatic erythrocytes was detected in male or female B6C3F1 mice given allyl alcohol by gavage at doses of up to 50 mg/kg bw/d for 13 weeks.

**Reliability:** (2) valid with restrictions  
GLP compliant, NTP guideline study but only limited information available for review, hence Reliability 2.

16-NOV-2003 (29)

**Type:** other: enhanced dominant lethal test (with karyotypic evaluation)

**Species:** rat **Sex:** male

**Strain:** Sprague-Dawley

**Route of admin.:** gavage

**Exposure period:** 33 wk

**Doses:** 25 mg/kg bw

**Result:** negative

**Method:** other: research investigation

**Year:** 1990

**GLP:** no

**Test substance:** as prescribed by 1.1 - 1.4

**Method:** ANIMALS AND TREATMENTS

Male SD rats (9-11 wk old) were given 0.85% saline (control group; n=6) or allyl alcohol (25 mg/kg bw/d) by oral gavage (10 ml/kg bw; 7 d/wk for 12 wk, 5 d/wk to wk 15).

Each male was caged with 2 virgin females (until a sperm-positive smear was obtained; up to 6 nights) on wk 1-11.

After mating was complete the males were subject to a gross postmortem examination and hematological screen. Sperm parameters were also assessed (no further methodological details). Males treated with allyl alcohol were sacrificed in wk 15, while controls were maintained until wk 33 (dosed 5 d/wk, in support of a parallel experiment).

#### REPRODUCTION PARAMETERS

On GD20, females from mating weeks 1-11 were killed and the uteri examined for:

- total number of corpora lutea
- total implants
- live / dead fetuses
- late / early deaths (calculated as a percentage of the total implants from the pregnant females in each group)

#### FETAL EXAMINATION

Each fetus was weighed and examined. Abnormal fetuses were photographed (polaroid) prior to removal of a sample of liver (chromosomal preparation) and preservation for skeletal staining and evaluation. The abnormal fetal index was calculated as a percentage of the total number of term fetuses observed at post-mortem. When karyotype abnormalities were observed the chromosome(s) involved were identified according to the standard karyotype of the Norway rat (Committee for a Standardised Karyotype of Rattus norvegicus; not included in study bibliography). (No further details are given on methods used for chromosomal and karyotypic analysis.)

#### STATISTICAL METHODS

Litter data were analyzed using Fisher's exact test. Other data were evaluated for significant differences relative to the controls, however the methods used are not reported. The authors note that paternal exposure to a mutagenic agent result in changes in chromosomal structure and/or number, which may be manifest as fetal abnormalities or changes in karyotype.

**Remark:**

Cyclophosphamide (3.5-5.1 mg/kg for up to 33 wk) was also evaluated in this study. It was associated with a highly significant and consistent increase in the numbers of malformed fetuses with karyotypic abnormalities. These effects were paralleled by a large increase in the number of post-implantation losses (dominant lethal events), but no significant effect on sperm parameters. These findings validate the methods used in this study.

**Result:**

#### PATERNAL EFFECTS

Mean body weight was lower in male rats given allyl alcohol (569+/-49 g) compared to controls (635+/-74g); this may, in part, have reflected the 18 wk age difference at sacrifice. Relative liver weight was increased 26% (P<0.05), and relative spleen weight 22% (P<0.05), with non-significant increases in relative kidney and testis weights (data not reported).

Red cell count, mean cell volume, percentage cell volume and hemoglobin concentration were unaffected by treatment with allyl alcohol (data not reported). White cell counts were similar in treated and control animals, however a differential count revealed a significant increase in percentage of lymphocytes with a corresponding significant decrease in eosinophils and neutrophil counts (data not reported). The authors comment that these changes in differential count were within the normal range for the SD rat.

Total sperm count and epididymal sperm concentration were unaffected by treatment (data not reported).

#### REPRODUCTION PARAMETERS

There was a total of 1669 live implants from 125 pregnancies in the controls (13.4 implants/litter) versus 1371 live implants from 108 litters in the allyl alcohol-treated group (12.7 implants/litter) (non significant).

Mean preimplantation loss was comparable in control (12.8+/-5.4%) and treated (11.7+/-6.2%) groups.

The rate of post-implantation loss (dominant lethality) varied between 2.2-13.2% in the controls, with a mean for the whole study (13 matings) of 6.2%. The comparable range for the male rats given allyl alcohol was 1.7-8.7%, with an overall mean of 4.7%.

#### FETAL ABNORMALITIES

The incidence of runted, abnormal and grossly abnormal fetuses was comparable in the control and treated groups.

	Control	Treated
Total number runts	13 (0.78%)	13 (0.95%)
Total number gross abnormalities (%)	0 (0%)	3 (0.22%)
Total number abnormal fetuses (%)	13 (0.78%)	16 (1.17%)

The three abnormalities in the treated group comprised were diagnosed as:

- anasarca (massive edema)
- exencephaly
- craniofacial and skeletal abnormality.

The combined incidence of gross abnormalities was not statistically significantly different between the control (n=0) and treated (n=3) groups.

Comment: The authors note that the incidence of grossly abnormal fetuses (0.22%) was within the historic range for this strain of rat (not reported) and were therefore considered to be spontaneous in origin.

#### KARYOTYPIC ANALYSIS

Karyotypic abnormalities were present in 3 of 12 slides prepared from abnormal fetuses from the treated group whereas no abnormal karyotype was present in 5 slides from the controls:

	Control	Treated
No. of abnormal fetuses evaluated:	8	14
Slides with scorable metaphases:	5	12
Slides with no karyotypic abnormality	5	9
Slides with karyotypic abnormality	0	3

The abnormalities from the allyl alcohol treated group were diagnosed as:

- trisomy with 3 fragments of possible centromeric origin in every metaphase (runt)
- trisomy (anasarca/runt)
- trisomy (craniofacial/skeletal)

Comment: Data for other endpoints described in the methods section are not reported in the paper; it is assumed that these were unaltered by treatment with allyl alcohol.

**Test substance:** Allyl alcohol, Aldrich Chemical Co., Gillingham, Dorset, UK (no further details).

**Conclusion:** Under the conditions of the study, no increase in post-implantation loss (dominant lethality) or chromosomal/karyotypic abnormalities were present in fetuses sired by male SD rats given allyl alcohol at 25 mg/kg bw/d for up to 12 wk.

**Reliability:** (2) valid with restrictions  
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

04-NOV-2003

(18)

### 5.7 Carcinogenicity

**Species:** rat **Sex:** male/female  
**Strain:** Fischer 344  
**Route of administration:** drinking water  
**Exposure period:** 106 wk  
**Post exposure period:** until natural death  
**Doses:** 0 or 300 mg/l  
**Result:** negative  
**Control Group:** yes, concurrent vehicle

**Year:** 1987  
**GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** Male and female F344 rats (n=20/sex; age 7-8 wk; housed 4/cage) were given allyl alcohol (300 mg/l) in drinking water 5 d/wk for up to 106 wk (tap water given on remaining days). A similar number of animals received tap water ad libitum. The animals were allowed to survive until natural death or until wk 123-132 of the study, whichever occurred later.

Fresh solutions were prepared weekly and stored in a refrigerator until use. Stability studies (GC analysis)

demonstrated 100% recovery of allyl alcohol after 7 days (no further information available).

**Result:** No further experimental details available.  
Median survival was unaffected by treatment:  
- males: controls = 115 wk, treated = 113 wk  
- females: controls = 118 wk, treated = 112 wk

The tumors observed in this study were stated to be of the types commonly seen in untreated F344 rats. Findings were as follows:

**LIVER:**  
Hyperplastic nodules and a few well differentiated hepatocellular carcinoma.  
Controls: 2/20 M; 2/20 F  
Treated: 3/20 M; 6/20 F

**ADRENAL CORTEX:**  
Hyperplastic nodules and adenoma.  
Controls: 1/20 M; 1/20 F  
Treated: 0/20 M; 0/20 F

**PITUITARY:**  
No description.  
Controls: 14/20 M; 14/20 F  
Treated: 10/20 M; 10/20 F

**LEUKEMIA:**  
No description.  
Controls: 12/20 M; 6/20 F  
Treated: 8/20 M; 6/20 F

**Comment:** While the authors comment that the occurrence of specific tumor types was increased after treatment with other substances included in this study, the increased occurrence of hepatic nodules/carcinoma in females given allyl alcohol relative to that present in the controls is not the subject of discussion. This suggests this finding was considered of doubtful biological significance.

**Test substance:** Allyl alcohol, Aldrich Chemical Company (no further details).  
**Conclusion:** Under the conditions of this study, no clear evidence of carcinogenicity was seen in male or female F344 rats given allyl alcohol in drinking water (300 mg/l) for up to 106 wk.  
**Reliability:** (2) valid with restrictions  
Study available for review. Non-guideline, non-GLP study. Reasonably well reported methods but limited reporting of results. Supports overall hazard assessment.

**Species:** Syrian hamster **Sex:** male  
**Route of administration:** gavage  
**Exposure period:** 60 wk  
**Post exposure period:** until natural death  
**Doses:** 0 or 2 mg/day  
**Result:** negative  
**Control Group:** yes, concurrent vehicle

**Year:** 1987  
**GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4

**Remark:** In a poorly reported study, no increase in tumors of the adrenal cortex, forestomach or pancreas duct was noted in male Syrian hamsters give 2 mg allyl alcohol in corn oil for up to 60 wk. The animals were allowed to survive until natural death or for up to a further 30-32 wk post-treatment. Although not stated, it is assumed that gavage administration was employed.

**Test substance:** Allyl alcohol, Aldrich Chemical Company (no further details).  
**Reliability:** (4) not assignable  
Study available for review. Briefly reported methods and findings, insufficient for full assessment, reliability cannot be assessed.

17-OCT-2003

(22)

### 5.8.1 Toxicity to Fertility

**Type:** other  
**Species:** rat  
**Sex:** male  
**Strain:** Wistar  
**Route of administration:** drinking water  
**Exposure Period:** 15 wk

**Year:** 1978  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** ANIMALS AND TREATMENTS  
Groups of Wistar rats (15/sex/treatment level) were exposed to allyl alcohol in the drinking water at 0 (control), 50, 100, 200 or 800 ppm for 15 weeks.

#### NECROPSY AND HISTOPATHOLOGY

At the end of the appropriate treatment period, animals were killed by exsanguination following an overnight fast and subject to a post-mortem examination. This included gonadal weights and histopathological examination of testis, ovary and uterus.

**Result:** See Section 5.4 for further experimental details.  
INTAKE OF TEST SUBSTANCE  
The calculated mean intake of allyl alcohol over the course of

the study (based on body weight and water intake data) was:  
Males: 0, 4.8, 8.3, 14.0, 48.2 mg/kg bw/d  
Females: 0, 6.2, 6.9, 17.1 and 58.4 mg/kg bw/d

## POST MORTEM EXAMINATION

Absolute organ weights (including gonadal weights) were generally decreased in males, and to a lesser extent in females, in a time- and treatment related manner. Relative organ weights (including gonadal weights) were generally increased to a statistically significant extent in high dose animals of both sexes at study termination. These changes appeared secondary to a reduction in water intake (presumably due to unpalatability of the treatment solution) and body weight, that was particularly pronounced in high dose animals.

## HISTOPATHOLOGICAL EVALUATION

No histopathological abnormalities were reported for testis, ovary or uterus.

**Test substance:** Allyl alcohol, 99% pure, SG (20 degree C) 0.849-0.852; bpt 95-98 degrees C, supplied by Bush Boake Allen Ltd, London.  
**Conclusion:** No treatment-related changes were present in gonadal weights or histopathology in male and female rats given allyl alcohol at received doses of up to 48-58 mg/kg bwt/d.  
**Reliability:** (2) valid with restrictions  
Study available for review. Non-guideline, non-GLP study. Reasonably well reported methods and results, suitable for assessment.

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(5)

**Type:** other  
**Species:** rat  
**Sex:** male  
**Strain:** Sprague-Dawley  
**Route of administration:** gavage  
**Exposure Period:** up to 15 wk  
**Frequency of treatment:** 7 d/wk  
**Premating Exposure Period**  
  **male:** up to 11 wk  
  **female:** untreated  
**Method:** other: research investigation  
**Year:** 1990  
**GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4

**Method:** ANIMALS AND TREATMENTS  
Male SD rats (9-11 wk old) were given 0.85% saline (control group; n=6) or allyl alcohol (25 mg/kg bw/d) by oral gavage (10 ml/kg bw; 7 d/wk for 12 wk, then 5 d/wk to wk 15).  
Each male was caged with 2 virgin females (until a sperm-positive smear was obtained; up to 6 nights) on wk 1-11.

After mating was complete the males were subject to a gross postmortem examination. Gonadal weights and sperm parameters (no further methodological details) were assessed. Males treated with allyl alcohol were sacrificed in wk 15, while controls were maintained until wk 33 (dosed 5 d/wk, in support of a parallel experiment).

#### REPRODUCTION PARAMETERS

On GD20, females from mating weeks 1-11 were killed and the uteri examined for:

- total number of corpora lutea
- total implants
- live / dead fetuses
- late / early deaths (calculated as a percentage of the total implants from the pregnant females in each group)

#### STATISTICAL METHODS

Litter data were analyzed using Fisher's exact test. Other data were evaluated for significant differences relative to the controls, however the methods used are not reported.

#### Result:

#### PATERNAL EFFECTS

Mean body weight was lower in male rats given allyl alcohol (569 $\pm$ 49 g) compared to controls (635 $\pm$ 74g); this may, in part, have reflected the 18 wk age difference at sacrifice.

Relative testis weights were increased (data not reported; non-significant).

Total sperm count and epididymal sperm concentration were unaffected by treatment (data not reported).

#### REPRODUCTION PARAMETERS

There was a total of 1669 live implants from 125 pregnancies in the controls (13.4 implants/litter) versus 1371 live implants from 108 litters in the allyl alcohol-treated group (12.7 implants/litter) (non significant).

Mean preimplantation loss was comparable in control (12.8 $\pm$ 5.4%) and treated (11.7 $\pm$ 6.2%) groups.

Comment: Data for other endpoints described in the methods section are not reported in the paper; it is assumed that these were unaltered by treatment with allyl alcohol.

#### Test substance:

Allyl alcohol, Aldrich Chemical Co., Gillingham, Dorset, UK (no further details).

#### Conclusion:

Under the conditions of the study, no statistically significant changes were present in relative testis weight, total sperm count and epididymal sperm concentration or reproductive performance for male SD rats given allyl alcohol at 25 mg/kg bw/d for up to 12 wk.

#### Reliability:

(2) valid with restrictions  
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods but limited reporting of results. Supports overall hazard

04-NOV-2003 assessment.

(18)

### 5.8.2 Developmental Toxicity/Teratogenicity

Species: rat Sex: female  
Strain: Sprague-Dawley  
Route of administration: other: intraamniotic injection

Year: 1985  
GLP: no  
Test substance: as prescribed by 1.1 - 1.4

**Method:** Time-mated pregnant SD rats (225-250; Charles River Canada Inc.) were anesthetized (ether) on GD13 and the uteri exposed. Embryos in one uterine horn received an intraamniotic injection (10 ul; 30-gauge needle) of allyl alcohol (10, 100 or 1000 ug/fetus in 0.9% NaCl) while those in the other horn were untreated. An unspecified number of saline injected controls were also included in the study and treated in a similar manner (ie injected or sham treated). The uterus was repositioned and the laporotomy closed (nylon sutures).

Rats were sacrificed on GD20 (ether overdose) and the number of dead or resorbed fetuses recorded. Live fetuses were examined for external malformations, blotted dry and weighed.

**Result:** The results were analyzed using the Mann-Whitney U-Test. Approx. 24% of the saline-injected control fetuses and 12% of the sham control fetuses were resorbed; 6% or 5%, respectively, were malformed. Comment: The number of control litters is not reported.

Allyl alcohol treatment was associated with a dose-related increase in resorptions (treated uterine horn versus untreated contralateral horn), which was significant in the intermediate and high treatment groups. While no tabulated results are available, interpolation from graphical data included in the publication indicates that the mean number of dead or resorbed fetuses was 0.3, 0.5 (P<0.05) and 0.6 (P<0.05) in the 10 (5 litters), 100 (8 litters) and 1000 (7 litters) ug/fetus groups.

Comment: The occurrence of dead or resorbed fetuses also increased in a treatment-related manner in the fetuses from the contra-lateral (untreated) uterine horn : <0.1, 0.2, 0.4 for the low, intermediate and high dose groups.

Two fetuses from 7 high dose litters were malformed (limb defects; non-significant). Two contralateral controls (untreated) from 8 intermediate dose litters were also malformed (omphalocele, edema, micromelia of the limbs, clubfoot, short neck and micrognathia; the other had a minor forelimb defect).

**Test substance:** Allyl alcohol, Aldrich Ltd, Montreal, Canada (no further details).

**Conclusion:** A treatment related increase in dead and resorbed fetuses was reported following intraamniotic injection of 100 or 1000 ug allyl alcohol/fetus on GD13. However the non-physiological route of exposure, together with an increased occurrence of dead/resorbed fetuses in the untreated (contra-lateral) uterine horn, suggests these observations are of doubtful reliability for the purposes of hazard identification.

**Reliability:** (4) not assignable  
Study available for review. Briefly reported methods and findings, insufficient for full assessment, reliability cannot be assessed.

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(34)

### 5.8.3 Toxicity to Reproduction, Other Studies

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### 5.9 Specific Investigations

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### 5.10 Exposure Experience

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5. Toxicity

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Substance ID: 107-18-6

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**5.11 Additional Remarks**

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**6.1 Analytical Methods**

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**6.2 Detection and Identification**

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**7.1 Function**

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**7.2 Effects on Organisms to be Controlled**

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**7.3 Organisms to be Protected**

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**7.4 User**

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**7.5 Resistance**

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**8.1 Methods Handling and Storing**

**8.2 Fire Guidance**

**8.3 Emergency Measures**

**8.4 Possib. of Rendering Subst. Harmless**

**8.5 Waste Management**

**8.6 Side-effects Detection**

**8.7 Substance Registered as Dangerous for Ground Water**

**8.8 Reactivity Towards Container Material**

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**10.1 End Point Summary**

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**10.2 Hazard Summary**

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**10.3 Risk Assessment**

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