

201-15652B

**General Information**

CAS Number: 109-09-1  
Common Name: 2-Chloropyridine

**II. Physical-Chemical Data**

**A. Melting Point**

**Entry 1 of 2**

**Test Substance**

Identity: 2-Chloropyridine  
Remarks: Mean or weighted melting point

**Method**

Method: Estimation  
Remarks: None

**Results**

Melting Point Value: -12.6°C  
Remarks: None

**Reference**

MPBPWIN v1.40 (EPI Suite™ v.3.10).  
Downloadable at  
[http://www.epa.gov/oppt/exposure/docs/episuitedl.h](http://www.epa.gov/oppt/exposure/docs/episuitedl.htm)  
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**Other**

01:11:01 01:10:10  
01:11:01 01:10:10

## Melting Point

### Entry 2 of 2

#### Test Substance

Identity: 2-Chloropyridine  
Remarks: Calculated value as listed on company data sheet.

#### Method

Method: Not stated.  
Remarks: None

#### Results

Melting Point Value: -46°C  
Remarks: None

#### Conclusions

The water solubility was provided by a reliable resource. The endpoint has been adequately characterized.

#### Data Quality

Reliability: 2D  
Remarks: Reliable with restrictions; information provided from a reliable reference.

#### Reference

Material Safety Data Sheet for 2-chloropyridine. Chemicaland21. Seoul, 150-010 Korea.

#### Other

## **B. Boiling Point**

### **Entry 1 of 2**

#### **Test Substance**

Identity: 2-Chloropyridine  
Remarks: None

#### **Method**

Method: Estimation  
Remarks: Adapted from Stein & Brown method

#### **Results**

Boiling Point Value: 150.07°C  
Remarks: None

#### **Reference**

MPBPWIN v1.40 (EPI Suite™ v.3.10).  
Downloadable at  
[http://www.epa.gov/oppt/exposure/docs/episuitedl.h](http://www.epa.gov/oppt/exposure/docs/episuitedl.htm)  
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#### **Other**

## Entry 2 of 2 for Boiling Point

### Test Substance

Identity: 2-Chloropyridine  
Purity: Not stated  
Remarks: None

### Method

Method: Not stated  
GLP: Not stated  
Year: Not stated  
Remarks: None

### Results

Boiling Point Value: 170°C  
Remarks: None

### Conclusions

The boiling point was provided in a reliable resource book. The endpoint has been adequately characterized.

### Data Quality

Reliability: 2D  
Remarks: Reliable with restrictions; endpoint was provided in a reliable reference text.

### Reference

Sax, N. I. and R. J. Lewis, Sr. 1987. Hazardous Chemicals Desk Reference. Pp. 332-333. Van Nostrand Reinhold Co., NY, NY.

### Other

## **F. Vapor Pressure**

### **Entry 1 of 2**

#### **Test Substance**

Identity: 2-Chloropyridine  
Remarks: None

#### **Method**

Method: Estimation  
Remarks: Mean of Antoine and Grain methods

#### **Results**

Vapor Pressure Value: 1.56 mmHg @ 25°C  
Remarks: None

#### **Reference**

MPBPWIN v1.40 (EPI Suite™ v.3.10).  
Downloadable at  
[http://www.epa.gov/oppt/exposure/docs/episuitedl.h](http://www.epa.gov/oppt/exposure/docs/episuitedl.htm)  
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#### **Other**

## Entry 2 of 2 for Vapor Pressure

### Test Substance

Identity: 2-Chloropyridine  
Remarks: None

### Method

Method: Stated in reference text  
Remarks: None

### Results

Vapor Pressure Value: 1.0 mmHg @ 13.3°C  
5.0 mmHg @ 38.8°C  
Remarks: None

### Reference

Perry's Chemical Engineers' Handbook. D. W. Green, ed. 6<sup>th</sup> edition. McGraw-Hill Company, New York. 1984.

### Other

## D. Partition Coefficient – Entry 1 of 2

### Test Substance

Identity: 2-Chloropyridine  
Remarks: None

### Method

Method: Estimation  
Remarks: None

### Results

$K_{ow}$ : 1.45  
Remarks: None

### Reference

KOWWIN v.1.66. (EPI Suite™ v.3.10).  
Downloadable at  
[http://www.epa.gov/oppt/exposure/docs/episuitedl.h](http://www.epa.gov/oppt/exposure/docs/episuitedl.htm)  
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### Other

## Entry 2 of 2 for Partition Coefficient

### Test Substance

Identity: 2-Chloropyridine  
Purity: Not stated  
Remarks: None

### Method

Method: Not stated  
GLP: Not stated  
Year: Not stated  
Remarks: None

### Results

$K_{ow}$ : 1.22  
Temperature: Not stated  
Remarks: None

### Conclusions

The partition coefficient was provided in a reliable resource book. The endpoint has been adequately characterized.

### Data Quality:

Reliability: 2D  
Remarks: Reliable with restrictions; information provided in a reliable reference text.

### Reference

Hansch, C., Leo, A. and Hoekman, D. 1995. Exploring QSAR: Hydrophobic, Electronic and Steric Constants. American Chemical Society. ACS Professional Reference Book, ACS, Washington, DC.

### Other

## E. Water Solubility

### Entry 1 of 2

#### Test Substance

Identity: 2-Chloropyridine  
Remarks: None

#### Method

Method: Estimation  
Remarks: None

#### Results

Value: 9,609 mg/l  
Temperature: 25°C  
Remarks: A  $K_{ow}$  of 1.22 was used in this estimation.

#### Reference

WSKOW v1.40 (EPI Suite™ v.3.10).  
Downloadable at  
[http://www.epa.gov/oppt/exposure/docs/episuitedl.h](http://www.epa.gov/oppt/exposure/docs/episuitedl.htm)  
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#### Other

## Entry 2 of 3 for Water Solubility

### Test Substance

Identity: 2-Chloropyridine  
Purity: Not stated  
Remarks: None

### Method

Method: Not stated  
GLP: Not stated  
Year: Not stated  
Remarks: None

### Results

Value: 2,000 mg/l  
Temperature: 25°C  
Remarks: None

### Conclusions

The water solubility was provided in a reliable resource book. The endpoint has been adequately characterized.

### Data Quality

Reliability: 2D  
Remarks: Reliable with restrictions; information provided in a reliable reference text.

### Reference

Lide, D. R. and Frederikse, H. P. R., eds. CRC Handbook of Chemistry and Physics, 75<sup>th</sup> ed. CRC Press, Boca Raton, FL. 1995.

### Other

### Entry 3 of 3 for Water Solubility

#### Test Substance

Identity: 2-Chloropyridine  
Purity: Not stated  
Remarks: None

#### Method

Method: Not stated  
GLP: Not stated  
Year: Not stated  
Remarks: None

#### Results

Value: 27,000 mg/l  
Temperature: 25°C  
Remarks: None

#### Conclusions

The water solubility was provided by a reliable resource. The endpoint has been adequately characterized.

#### Data Quality

Reliability: 2D  
Remarks: Reliable with restrictions; information provided from a reliable reference.

#### Reference

Material Safety Data Sheet for 2-chloropyridine. Chemicallyland21. Seoul, 150-010 Korea.

#### Other

### III. Environmental Fate Endpoints

#### A. Photodegradation

##### Test Substance

Identity: 2-Chloropyridine  
Remarks: None

##### Method

Method: Estimation  
Test type: Atmospheric oxidation  
Remarks: None

##### Results

Hydroxyl radicals  
reaction:  
OH Rate  
Constant:  $0.2603 \times 10^{-12} \text{ cm}^3/\text{molecule-sec}$   
Half-life: 41.094 days (12-hr day;  $1.5 \times 10^6 \text{ OH}/\text{cm}^3$ )  
Temperature:  $25^{\circ}\text{C}$   
Ozone reaction: No ozone reaction estimation was noted.  
Remarks: None

##### Conclusions

The material is expected to slowly degrade in the atmosphere.

##### Reference

AopWin v1.90. (EPI Suite™ v.3.10). Downloadable at  
[http://www.epa.gov/oppt/exposure/docs/episuitedl.h](http://www.epa.gov/oppt/exposure/docs/episuitedl.htm)  
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##### Other

## B. Stability in Water

### Test Substance

Identity:	2-Chloropyridine
Remarks:	None

The computer modeling program can not estimate the rate constants for aqueous acid/base-catalyzed hydrolysis. Although hydrolysis cannot be predicted using a computer estimation model, 2-chloropyridine does not have a site in which the water molecule or hydroxide ion can displace an atom or group of atoms. Chemical hydrolysis at a pH normally found in the environment, i.e. 5 to 9, can be important for a variety of chemicals that have functional groups that are potentially hydrolysable, such as amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters. It is the position of Arch Chemicals that data for this endpoint is not necessary since this chemical does not possess a structure that is hydrolysable. The judgment is that 2-PCI would be resistant to acid/base-catalyzed hydrolysis.

### C. Biodegradation – Entry 1 of 6

#### Test Substance

Identity: 2-Chloropyridine  
Purity: > 96%  
Remarks: Purchased from Sigma Chemical Co. St. Louis, MO

#### Method

Method: Non-specific test method for substrate depletion and methane formation in a sealed system.  
Test type: Anaerobic biodegradation in a sediment/water slurry.  
GLP: Not stated  
Year: 1994  
Contact time: 12 months  
Inoculum: Sediment and ground water collected from a methanogenic aquifer contaminated with landfill leachate.  
Remarks: Experiments were performed in triplicate and employed both sterile and substrate-unamended controls. In addition acetate and 3-chlorobenzene were employed as positive controls. The headspace of the test vessels was monitored for methane formation by gas chromatography (GC). Methane produced in unamended controls was subtracted from that produced in substrate-amended vessels and compared to the theoretically expected amount based on Buswell's equation and the initial substrate concentration. Substrate depletion and metabolite formation was monitored by reverse-phase high-pressure liquid chromatography (HPLC).

#### Results

Degradation: 2-Chloropyridine was not removed from the test system and evidence of mineralization was not observed.  
Results: No methane production was observed. Substrate recovery after 1 year of incubation was  $107 \pm 5\%$ . No intermediates were observed.  
Kinetic: Not stated  
Breakdown products: Not stated  
Remarks: None

#### Conclusions

The biodegradability of the test substance has been adequately characterized.

**Data Quality**

Reliability:

2A

Remarks:

Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

**Reference**

Adrian, N. R. and Sulfito, J. M. 1994. Anaerobic biodegradation of halogenated and nonhalogenated N-, S- and O-heterocyclic compounds in aquifer slurries. *Environ. Toxicol. Chem.* 13, 1551-1557.

**Other**

## Entry 2 of 6 for Biodegradation

### Test Substance

Identity: 2-Chloropyridine  
Purity: Not stated  
Remarks: Purchased from Sigma Chemical Co. St. Louis, MO

### Method

Method: Non-specific test method for substrate depletion.  
Test type: Anaerobic  
GLP: Not stated  
Year: 1995  
Contact time: 12 months  
Inoculum: Sediment and ground water collected from a freshwater pond contaminated with small particles of asphalt.  
Remarks: Experiments were performed in duplicate and employed both sterile and substrate-unamended controls. Substrate depletion and metabolite formation was monitored by HPLC.

### Results

Degradation: 2-Chloropyridine was not removed from the test system.  
Results: Some loss of 2-chloropyridine was observed; however, the loss was not significantly different from that in the corresponding sterile controls. No transformation was observed.  
Kinetic: Not stated  
Breakdown products: Not stated  
Remarks: None

### Conclusions

The biodegradability of the test substance has been adequately characterized.

### Data Quality

Reliability: 2A  
Remarks: Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

### Reference

Lui, S. M. 1995. Anaerobic dechlorination of chlorinated pyridines in anoxic freshwater sediment slurries. J. Environ. Sci. Health. A30, 485-503.

### Other

### Entry 3 of 6 for Biodegradation

#### Test Substance

Identity: 2-Chloropyridine  
Purity: Not stated  
Remarks: Purchased from Aldrich Chemical Co.

#### Method

Method: Assessment of degradation based on substrate depletion.  
Test type: Anaerobic biodegradation  
GLP: Not stated  
Year: 1989  
Contact time: 200 days  
Inoculum: Sediment and overlying site water from an estuary.  
Remarks: Biodegradation of 2-chloropyridine was evaluated in sediment slurries (10% solids) under sulfate reducing conditions. Experiments were replicated and included control sediments. Testing was conducted at 78.8  $\mu\text{M}$ . Test chambers were incubated in the dark at 23-25°C. Samples for analysis were removed using a syringe and needle periodically. Substrate concentration was measured using HPLC.

#### Results

Degradation: None reported  
Results: 2-Chloropyridine was persistent in the anoxic sediment.  
Kinetic: Not stated  
Breakdown products: Not stated  
Remarks: None

#### Conclusions

The biodegradability of the test substance has been adequately characterized.

#### Data Quality

Reliability: 2B  
Remarks: Reliable with restrictions; basis data given, comparable to guidelines/standards.

#### Reference

Lui, S. M., Wu, C. H. and Huang, H. J. 1989. Toxicity and anaerobic biodegradability of pyridine and its derivatives under sulfidogenic conditions. Chemosphere 10, 2345-2357.

#### Other

## Entry 4 of 6 for Biodegradation

### Test Substance

Identity: 2-Chloropyridine  
Purity: Not stated  
Remarks: None

### Method

Method: Non-guideline specific study of biodegradation of the test substance in soil suspensions.

Test type: Aerobic biodegradability

GLP: No

Year: 1986

Contact time: 24 days

Inoculum: Soil suspension

Remarks: Degradation experiments were carried out in 500-ml Erlenmeyer flasks. Flasks were prepared to contain 150 ml of basal salts medium amended with yeast extract and potassium phosphate buffer adjusted to pH 7.0. To each replicate flask (note – replication noted in article, but the number of replicates was not specified) 1 ml of 2-chloropyridine solution was added to give a final substrate concentration of approximately 1 mM. Flasks were inoculated with 1 ml of a dilute soil suspension prepared by suspending 15 g soil (Fincastle silt loam) in 1 l of mineral salts medium and continuously stirring while 1-ml aliquots were removed. Flasks were incubated at 24°C for up to 30 days. Subsamples were removed from each flask before and after inoculation and periodically throughout the incubation. 2-Chloropyridine concentrations were monitored by UV spectrophotometry during the incubation period. The disappearance of 2-chloropyridine from solutions plus the mineralization of pyridine-N was taken as evidence of degradation.

### Results

Degradation: UV analysis indicated a 47% loss of 2-chloropyridine from the test solutions by 24 days, while inorganic nitrogen released to the test solutions accounted for <1% degradation.

Results: 2-Chloropyridine did not appear to be appreciable degraded. The amount of 2-chloropyridine lost

from the test solutions determined by UV analysis was 47% within 24 days. Less than 1% was determined to be biodegraded based on release of inorganic nitrogen in the test solutions, while 37% was lost through volatilization and 3.2% adsorbed by soil.

Kinetic: Not stated  
Breakdown products: Not stated  
Remarks: None

**Conclusions**

The biodegradability of the test substance has been adequately characterized.

**Data Quality**

Reliability: 2A  
Remarks: Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

**Reference**

Sims, G. K. and Sommers, L. E. 1986.  
Biodegradation of pyridine derivatives in soil suspensions. Environ. Toxicol. Chem. 3, 503-509.

**Other**

## Entry 5 of 5 for Biodegradation

### Test Substance

Identity: 2-Chloropyridine  
Purity: Not stated  
Remarks: None

### Method

Method: Non-specific method measuring substance depletion and inorganic N released.  
Test type: Aerobic biodegradation in soil  
GLP: Not stated  
Year: 1985  
Contact time: 64 days  
Inoculum: The test soil was a Fincast silt loam which had a pH of 6.7, organic carbon content of 12 g/kg, total N content of 1300 mg/kg, CEC of 0.15 mol (+)/kg and contained 0.25 kg H<sub>2</sub>O/kg dry soil as – 0.03 MPa.  
Remarks: Test chambers were prepared in duplicate and dosed at 200 mmol/kg. At 3- and 4-day intervals the soils were adjusted for loss of moisture. After 0, 1, 2, 4, 8, 16, 32 and 64 days of incubation, the foam stoppers and soil from replicate chambers were extracted and analyzed. In addition, a sterile treatment was extracted and analyzed after 7 days of incubation.

### Results

Degradation: 89% of the test substance remained in the soil after 64 days of incubation, indicating little biodegradation of the test substance occurred over the study period. This was confirmed by little inorganic nitrogen accumulation during incubation.  
Results: The measured day 0 concentration of the test substance was 113.7% of the nominal concentration. After 64 days of incubation, 89% of the test substance remained in the soil. Accumulation of inorganic nitrogen at days 16, 32 and 64 was equivalent to 1.3, < 0.1 and <0.1% of the extractable test substance.  
Kinetic: Not stated  
Breakdown products: Not stated  
Remarks: None

### Conclusions

The biodegradability of the test substance has been adequately characterized.

**Data Quality:**

Reliability:

2A

Remarks:

Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

**Reference**

Sims, G. K. and Sommers, L. E. 1985. Degradation of pyridine derivatives in soil: Chemical and biological assessment. J. Environ. Qual. 14, 580-584.

**Other**

## Entry 5 of 5 for Biodegradation

### Test Substance

Identity: 2-Chloropyridine  
Purity: Not stated  
Remarks: None

### Method

Method: Not stated  
Test type: Aerobic biodegradation in activated sludge  
GLP: Not stated  
Year: 1992  
Contact time: 14 days  
Inoculum: Activated sludge  
Remarks: Concentration of test substance – 100 mg/l  
Concentration of activated sludge – 30 mg/l  
Volume of test solution – 300 mg/l  
Cultivation temperature – 25°C

### Results

Results: After 14 days in contact with the activated sludge there was no evidence of biodegradation.  
Breakdown products: Not stated  
Remarks: None

### Conclusions

2-Chloropyridine is resistant to biodegradation from activated sludge.

### Data Quality:

Reliability: 2B  
Remarks: Reliable with restrictions; basic data given, comparable to guidelines/standards.

### Reference

Chemicals Inspection and Testing Institute.  
Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan; Japan Chemical Industry Ecology-Toxicology and Information Center, ISBN 4-89074-101-1 pp. 3-42 (1992).

### Other

## D. Transport between Environmental Compartments (Fugacity)

### Test Substance

Identity: 2-Chloropyridine  
Remarks: None

### Method

Method: Estimation  
Model: Level III Fugacity Model  
Remarks: None

### Results

Estimated distribution and media concentration:		Mass Amount (%)	Half-Life (hr)	Emissions (kg/hr)
	Air	7.52	986	1000
	Water	48.8	900	1000
	Soil	43.6	900	1000
	Sediment	0.104	$3.6 \times 10^3$	0

Remarks: Physical chemical values utilized in this model were default values obtained from the EPIWIN program.  
Input values for calculation

- Molecular weight – 133.55
- Vapor pressure – 5 mmHg
- Log  $K_{ow}$  – 1.22
- Water solubility – 27,000 mg/l
- Melting point –  $-46^{\circ}\text{C}$
- Boiling point –  $170^{\circ}\text{C}$
- Henry's LC –  $1.63\text{e-}005 \text{ atm}\cdot\text{m}^3/\text{mole}$

### Reference

Level III Fugacity Model. (EPI Suite™ v.3.10).  
Downloadable at  
<http://www.epa.gov/oppt/exposure/docs/episuitedl.htm>  
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### Other

#### IV. Ecotoxicity

##### A. Acute Toxicity to Fish

###### Test Substance

Identity: 2-Chloropyridine  
Remarks: None

###### Method

Method: Estimation  
Test type: 96-hour LC<sub>50</sub>  
Organism: Fish  
Remarks: None

###### Results

LC<sub>50</sub> (96 hours): 277 mg/l  
Remarks: None

###### Reference

Nabholz, J. V., Cash, G., Meylan, W. M. and Howard, P. H. 2001. ECOSAR: A Computer Program for Estimating the Ecotoxicity of Industrial Chemicals Based on Structure Activity Relationships, Version 0.99g. Washington, DC: Risk Assessment Division, Office of Pollution Prevention and Toxics, United States Environmental Protection Agency. Available from EPA web page at <http://www.epa.gov/oppt/newchems/21ecosar.htm> or <http://www.epa.gov/oppt/exposure/docs/episuitd.htm>

###### Other

## A. Acute Toxicity to Fish

### Test Substance

Identity: 3-Methylpyridine (CAS RN 108-99-6)  
Purity: Not stated  
Remarks: None

### Method

Method: OECD Guideline 203  
Test type: Acute, static renewal  
GLP: Yes  
Year: 1991  
Species/Strain/  
Supplier: Zebra fish (*Brachydanio rerio*)/Not stated/Local  
fish hatchery

Analytical monitoring: No

Exposure period: 96 hours

Statistical methods: None

Remarks: The study measured the acute toxicity of the test substance to Zebra fish during a 96-hour static-renewal exposure period. Fish in holding tanks were fed a commercial fish food. Fish were acclimated to the water used in the test for 12 days prior to testing. Mean body weight and mean length of 30 fish used in testing were 0.42 g and 3.3 cm, respectively. Dilution water was reconstituted water made according to EEC directive. Dilution water characteristics were within the EEC directives for pH ( $7.9 \pm 0.3$ ), dissolved oxygen ( $\geq 74$  % saturation at  $20^\circ\text{C}$ ) and hardness ( $250 \pm 50$  mg/l as  $\text{CaCO}_3$ ). Test vessels were 8.3-l all-glass aquarium filled with 5 l of dilution water. They were fitted with aeration tubes, covered with a glass pane during the test and held in a water-bath at  $22 \pm 2^\circ\text{C}$  under a 16 hour light/8 hour dark photoperiod. Solutions of the substance were prepared by adding an aliquot of a 10 g test substance/l of stock solution to each test chamber. Test solutions were prepared fresh each day of the test. The pH, dissolved oxygen concentration and temperature of the test media were measured at the beginning and the end of the test. Fish were inspected at the beginning of the test and after approximately 2, 4, 24, 48, 72 and 96 hours for lethality and any behavior different from the control group.

**Results**

Nominal concentrations: 0, 100, 180, 320, 560 and 1000 mg/l  
Measured concentrations: Not measured  
LC<sub>50</sub> (96 hours): Greater than 560 but less than 1000 mg/l  
Remarks: The 96-hour NOEC with respect to behavior was 320 mg/l and the 96-hour NOEC with respect to mortality was 560 mg/l.

**Conclusion**

The acute toxicity of the test substance has been adequately characterized.

**Data Quality**

Reliability: 1A  
Remarks: Reliable without restriction; OECD guideline study

**Reference**

Weytjens, D. and R. Wils. 1991. The Acute Toxicity of beta-Picoline (3-Methylpyridine) in the Zebra Fish (*Brachydanio rerio*). Reilly Industries, Indianapolis, IN.

**Other**

## B. Acute Toxicity to Daphnids

### Test Substance

Identity: 2-Chloropyridine  
Remarks: None

### Method

Method: Estimation  
Test type: 48-hour LC<sub>50</sub>  
Organism: Daphnid  
Remarks: None

### Results

LC<sub>50</sub> (48 hours): 286 mg/l  
Remarks: None

### Reference

Nabholz, J. V., Cash, G., Meylan, W. M. and Howard, P. H. 2001. ECOSAR: A Computer Program for Estimating the Ecotoxicity of Industrial Chemicals Based on Structure Activity Relationships, Version 0.99g. Washington, DC: Risk Assessment Division, Office of Pollution Prevention and Toxics, United States Environmental Protection Agency. Available from EPA web page at <http://www.epa.gov/oppt/newchems/21ecosar.htm> or <http://www.epa.gov/oppt/exposure/docs/episuiteld.htm>

### Other

## Acute Toxicity to Daphnids

### Test Substance

Identity: 3-Methylpyridine (CAS RN 108-99-6)  
Purity: Not stated  
Remarks: None

### Method

Method: OECD Guideline 202  
Test type: Acute static  
GLP: Yes  
Year: 1991  
Species/Strain/  
Supplier: *Daphnia magna* Straus/Not stated/State University  
of Ghent  
Analytical monitoring: No  
Exposure period: 48 hours  
Statistical methods: No statistics applied to data  
Remarks: Dilution water was reconstituted water prepared according to ISO-6341, 1982, with micronutrients. The pH was  $7.7 \pm 0.1$ , the water was oxygen-saturated and the hardness was  $250 \pm 25$  mg/l as  $\text{CaCO}_3$ . Daphnids were < 24 hours old at the start of the test. Test vessels were 80-ml all glass tubes containing 50 ml of test solution. Test solutions were prepared by adding an aliquot of a stock solution (1.0077 g 3-methylpyridine/l) to the dilution water. Four replicate test tubes were used per concentration and each test tube held 5 daphnids. The pH, dissolved oxygen concentration and temperature of the test medium in each test tube were measured at the start and end of the test. At 24 and 48 hours of the test, daphnids were evaluated for immobility. Daphnids not able to swim within 15 seconds after gentle agitation of the test tube were considered immobile.

### Results

Nominal concentrations: 0, 100, 180, 320, 560 and 1000 mg/l  
Measured concentrations: Not measured  
EC<sub>50</sub> (48 hour): 320 mg/l  
NOEC: 180 mg/l

**Conclusions**

The 48-hour acute toxicity of the test substance to *Daphnia magna* has been adequately characterized.

**Data Quality**

Reliability:

1A

Remarks:

Reliable without restriction; OECD guideline study

**Reference**

Weytjens, D. and R. Wils. 1991. The Acute Toxicity of beta-Picoline (3-Methylpyridine) in the Water flea (*Daphnia magna*). Reilly Industries, Indianapolis, IN.

**Other**

### C. Acute Toxicity to Aquatic Plants

#### Test Substance

Identity: 2-Chloropyridine  
Remarks: None

#### Method

Method: Estimation  
Test type: 96-hour EC<sub>50</sub>  
Organism: Green Algae  
Remarks: None

#### Results

EC<sub>50</sub> (96 hours): 173 mg/l  
Remarks: None

#### Reference

Nabholz, J. V., Cash, G., Meylan, W. M. and Howard, P. H. 2001. ECOSAR: A Computer Program for Estimating the Ecotoxicity of Industrial Chemicals Based on Structure Activity Relationships, Version 0.99g. Washington, DC: Risk Assessment Division, Office of Pollution Prevention and Toxics, United States Environmental Protection Agency. Available from EPA web page at <http://www.epa.gov/oppt/newchems/21ecosar.htm> or <http://www.epa.gov/oppt/exposure/docs/episuiteld.htm>

#### Other

## Acute Toxicity to Aquatic Plants (Algae)

### Test Substance

Identity: 3-Methylpyridine (CAS RN 108-99-6)  
Purity: Not stated  
Remarks: None

### Method

Method: OECD Guideline 201  
Test type: Acute static growth inhibition  
GLP: Yes  
Year: 1991  
Species/Strain/  
Supplier: *Selenastrum capricornutum*/CCAP 278-4/CCAP,  
UK  
Analytical monitoring: No  
Exposure period: 72 hours  
Statistical methods: No statistics applied to data  
Remarks: The growth medium used in the test was prepared according to the OECD guideline. The medium was filter-sterilized with a 0.45 µm membrane filter. The algae were cultured at the testing facility for several weeks in Boltz Basal Medium (BBM). Test vessels were all-glass 100-ml Erlenmeyer flasks containing 50 ml of test solution. Triplicate flasks were used at each test concentration. Test solutions were prepared by adding an aliquot from each of five stock solutions (1, 3.2, 10, 32 and 100 g test substance/l) to the appropriate test flasks. Flasks were inoculated with algal cells to achieve an initial cell density of 10<sup>4</sup> cells/ml. Flasks were incubated in an environmental cabinet under continuous illumination at a temperature of 25 ± 1 °C. Flasks were continuously shaken during the experiment. Cell counts were made after 3 days of incubation using a Neubauer counting chamber. The average specific growth rate was calculated for each flask and the average growth rate for each treatment was compared to the control group. The pH of the test solutions was measured in each flask at the beginning and end of the test.

### Results

Nominal  
concentrations: 0, 10, 32, 100, 320 and 1000 mg/l

Measured concentrations:  
EC<sub>50</sub> (72-hour):

Not measured  
320 mg/l

**Conclusions**

The 72-hour acute toxicity of the test substance to *Selenastrum capricornutum* has been adequately characterized.

**Data Quality**

Reliability:  
Remarks:

1A  
Reliable without restriction; OECD guideline study

**Reference**

Weytjens, D. and R. Wils. 1991. The Effect of beta-Picoline (3-Methylpyridine) on the Growth of Unicellular Green Algae (*Selenastrum capricornutum*). Reilly Industries, Indianapolis, IN.

**Other**

## V. Mammalian Toxicity

### A. Acute Toxicity – Entry 1 of 5

#### Test Substance

Identity: 2-Chloropyridine  
Purity: Not determined  
Remarks: None

#### Method

Method: Not stated  
Type: LD<sub>50</sub>  
GLP: No  
Year: 1964  
Species/Strain: Rat/Manor Wistar  
Sex: Male  
Number of animals/  
sex/dose: 6  
Vehicle: Methylcellulose  
Route of  
administration: Oral (gavage)  
Remarks: Groups of 6 male rats were administered a single dose of the test substance suspended in a 0.5% aqueous dispersion of methylcellulose via oral gavage at concentrations of 100, 215, 464, 681, 1000, 1470 and 2150 mg/kg. Each dose level was prepared in a concentration that enabled the delivery of a constant volume of 1.0 ml/100 g of body weight. Rats were in the weight range of 201-304 g. Food was withheld from all rats for 16 hours prior to dosing. Food and water were available *ad libitum* at all other times. Rats were observed for signs of toxicity and mortality continuously for 4 hours post-dose, at 24 hours post dose and once daily thereafter for 13 days. At the termination of the 14-day observation period, surviving rats were sacrificed. Necropsies were performed on all rats.

#### Results

Value: LD<sub>50</sub> – 342 mg/kg (confidence limits – 211 – 558 mg/kg)

Mortality rate:	Dose (mg/kg)	Mortality
	100	0/6
	215	1/6
	464	5/6
	681	6/6
	1000	6/6

1470	6/6
2150	6/6

Remarks:

At 16 hours post-dose, 4 rats in the 100 mg/kg dose group exhibited nasal porphyrin. At 24 hours post-dose, 4 rats appeared hypoactive. All animals appeared normal thereafter until study termination. Two rats in the 215 mg/kg dose group exhibited nasal porphyrin discharge at 4 hours post-dose. At 24 hours post-dose 4 rats were ataxic, sedate, hypoactive and displayed nasal porphyrin discharge. At 2 days all rats were hypoactive and continued to demonstrate nasal discharge. One animal was found dead on day 3. The remaining rats appeared normal throughout the remainder of the observation period. Within 6 hours 5 rats from the 464 mg/kg dose group exhibited ataxia and hypoactivity. One rat became prostrate. At 24 hours all rats were ataxic and exhibited nasal porphyrin. One rat was prostrate and dyspneic. At 2 days 1 rat died and 2 were ataxic and the remaining 3 appeared hypoactive. At 3 days all 5 rats were hypoactive and appeared depressed. At 4 days one died and the remaining 4 continued to be hypoactive and became hypersensitive to touch. Two more rats died on days 5 and 6. The remaining 2 rats were hypoactive and hypersensitive to touch. A fifth rat died. The remaining rat recovered and appeared normal from days 9 through 14. Rats in the 681, 1000, 1470 and 2150 mg/kg dose groups displayed hypotonia, ataxia, sedation, hypnosis, loss of righting reflex, pinna and placing reflexes, bradypnea, dyspnea, cyanosis, ptosis, salivation and reduced pain responses within 2 to 18 hours post-dose. Rats in all dose groups except the 681 mg/kg dose group died within 2 to 4 hours post-dose. Rats in the 681 mg/kg dose group died within 3 days. At necropsy, 1 rat in the 100 mg/kg dose group had hydronephrosis. The rat that died in the 215 mg/kg dose group exhibited a pale liver with friable accentuated lobules and the lungs were congested. Necropsy findings in the rats that died in the 464 mg/kg dose group included congested lungs, congested liver, hemorrhages of the stomach, small intestines and urinary bladder and icterus. All rats in the 100, 215 and 464 mg/kg dose groups that

survived to the 14-day post-exposure period had essentially normal necropsy findings. Necropsy findings in the 681, 1000, 1470 and 2150 mg/kg dose groups included scrotal erythema, hemorrhages of the stomach, intestines and urinary bladder and congested lungs and liver. Hydronephrosis (unilateral and bilateral) was scattered in all groups.

**Conclusions**

Remarks:

The acute oral LD<sub>50</sub> has been adequately characterized.

**Data Quality**

Reliability:

1B

Remarks:

Reliable without restriction; comparable to guideline study.

**Reference**

Wazeter, F. X. 1964. Acute Toxicity Studies in Rats and Rabbits. Report # 122-003. International Research and Development Corporation, Mattawan, MI.

**Other**

## Acute Toxicity – Entry 2 of 5

### Test Substance

Identity: 2-Chloropyridine  
Purity: > 97%  
Remarks: None

### Method

Method: “Sleeve” technique described by Draize et al. (1944) and Rowe et al. (1952). These references are cited in the study reference.  
Type: LD<sub>50</sub>  
GLP: No  
Year: 1966  
Species/Strain: Rabbit  
Sex: Male and female  
Number of animals/  
dose: 4-5  
Vehicle: None  
Route of  
administration: Dermal  
Remarks: Groups of male and female rabbits, weighing 1.3 to 2.3 kg, were exposed to the undiluted test substance dermally at concentrations of 40, 48, 50, 58, 63, 68, 79, 82 or 100 mg/kg.

### Results

Value: LD<sub>50</sub> – 64 mg/kg (confidence limits – 55.5 to 73.5 mg/kg)

Mortality rate:	Dose (mg/kg)	Mortality
	40	0/5
	48	1/4
	50	1/5
	58	2/5
	63	3/4
	68	2/5
	79	3/4
	82	3/5
	100	5/5

Remarks: The test substance caused only transient local congestion of the skin when applied to either intact or abraded skin. The primary gross lesion observed was hemorrhagic necrosis of the liver.

**Conclusions**

Remarks: The acute dermal LD<sub>50</sub> has been adequately characterized.

**Data Quality**

Reliability: 2A  
Remarks: Reliable with restriction; acceptable, well-documented publication which meets basic scientific principles.

**Reference**

Gehring, P. J., Torkelson, T. R. and Oyen, F. 1967. A Comparison of the Lethality of Chlorinated Pyridines and a Study of the Acute Toxicity of 2-Chloropyridine. Toxicol. Appl. Pharmacol. 11, 361-371.

**Other**

## Acute Toxicity – Entry 3 of 5

### Test Substance

Identity: 2-Chloropyridine  
Purity: Not determined  
Remarks: None

### Method

Method: Not stated  
Type: Acute dermal toxicity  
GLP: No  
Year: 1964  
Species/Strain: Rabbit  
Sex: Male and female  
Number of animals/  
sex/dose: 3  
Vehicle: None  
Route of  
administration: Dermal  
Remarks: Six rabbits (3 M; 3 F) per group, weighing between 2040 and 2828 g, were administered a single dose of the undiluted test substance dermally at concentrations of 200 and 2000 mg/kg. The back of each rabbit was clipped. The clipped back of 3 rabbits per group was abraded and the skin of the remaining 3 rabbits was left intact. The rabbits were exposed to the test substance for a period of 24 hours. The dosing site was not occluded during the 24 hour exposure period. Rabbits were observed frequently for pharmacotoxic effects during the first 4 hours after application, at 24 hours and once daily thereafter for a total of 14 days. The degree of dermal irritation and damage was evaluated. At the end of the observation period all surviving rabbits were weighed, sacrificed and necropsied. Rabbits that did not survive the observation period also were necropsied.

### Results

Value: LD<sub>50</sub> – < 200 mg/kg  
Mortality rate: 200 mg/kg – 5/6  
2000 mg/kg – 6/6

Remarks: Five rabbits in the 200 mg/kg dose group died within 18 to 40 hours post-dose. Death was preceded by cyanosis, bradypnea and dyspnea,

lacrimation, hypothermia and hypotonia of the skeletal musculature. One rabbit with intact skin survived. This rabbit demonstrated a very slight erythema of the area of application for the entire observation period. All rabbits in the 2000 mg/kg dose group died within 18 hours after displaying signs as noted above. Necropsy findings in the 200 mg/kg dose group included excessive mucous in the stomach and lungs that failed to collapse and which were congested and hemorrhagic. Fluid was found in the thoracic cavity and a strong odor of the test substance was present in the thoracic cavity. One rabbit displayed a hemorrhagic cecum. The surviving rabbit in this group exhibited no gross lesions. Necropsy findings in the 2000 mg/kg dose group included excessive mucous in the stomach and lungs that failed to collapse and which were congested and hemorrhagic. Foam was present in the trachea and major bronchi. A strong test substance odor was present in the thoracic cavity of all rabbits.

**Conclusions**

Remarks:

The acute dermal toxicity has been adequately characterized.

**Data Quality**

Reliability:

1B

Remarks:

Reliable without restriction; comparable to guideline study.

**Reference**

Wazeter, F. X. 1964. Acute Toxicity Studies in Rats and Rabbits. Report # 122-003. International Research and Development Corporation, Mattawan, MI.

**Other**

## Acute Toxicity – Entry 4 of 5

### Test Substance

Identity: 2-Chloropyridine  
Purity: > 97%  
Remarks: None

### Method

Method: Not stated  
Type: Acute inhalation toxicity  
GLP: No  
Year: 1966  
Species/Strain: Rat  
Sex: Female  
Number of animals/  
dose: 10-20  
Vehicle: None  
Route of  
administration: Inhalation  
Remarks: Groups of female rats, approximately 10 weeks old and weighing 132 to 190 g, were exposed to the test substance via inhalation at concentrations of 50, 100, 250, 500 and 1000 ppm for 0.1 to 7.0 hours. The concentration of 2-chloropyridine was monitored continuously during the exposure by infrared spectrophotometry. The degree and character of organic damage resulting from exposure to the test substance were the presence of gross pathologic or histopathologic lesions, hematologic alterations, organ weight changes and changes in the blood chemistry. Liver, kidney, spleen, heart, lungs and brain were examined for weight changes and together with pancreas and adrenals for the presence of histologic lesions. Hematologic studies consisted of erythrocyte, leukocyte and differential counts and hematocrit and hemoglobin determinations. Parameters used to detect changes in blood chemistry were blood urea nitrogen, serum glutamic-pyruvic transaminase and serum glutamic-oxalacetic transaminase. Rats were observed for 2 weeks post-exposure.

### Results

Value: LC<sub>50</sub> – > 100 ppm but < 250 ppm

Mortality rate:	Dose Level (ppm)	Length of Exposure (hrs)	Mortality Rate
	50	7.0	0/10
		4.0	0/10
	100	7.0	13/20
		4.0	7/20
		2.0	0/10
	250	7.0	12/12
		4.0	14/20
		2.0	8/10
		1.0	2/10
		0.5	0/10
	500	2.0	15/15
		1.0	8/15
		0.5	2/15
		0.2	0/14
	1000	1.0	14/15
		0.5	8/10
		0.2	8/17
		0.1	0/20

Remarks: The concentration of 2-chloropyridine vapor was within 7% of the desired concentration throughout the exposure period. Liver damage was the primary alteration caused by the inhalation of the test article. Histopathologic examinations revealed that the test substance caused central lobular necrosis, hemorrhage and fatty degeneration as well as cellular infiltration. The extent and type of damage varied with the exposure. Maximum single-dose exposures not causing these changes were 100 ppm for 3 minutes, 50 ppm for 6 minutes, 25 ppm for 12 minutes and 10 ppm for 30 minutes. Maximum single-dose exposures that did not cause death 1000 ppm for 6 minutes, 500 ppm for 12 minutes, 250 ppm for 30 minutes, 100 ppm for 2 hours and 50 ppm for 4 hours.

### Conclusions

Remarks: The LC<sub>50</sub> was not calculated, but based on the available data, the 4-hour LC<sub>50</sub> is between 100 and

250 ppm. Therefore, the acute inhalation LC<sub>50</sub> has been adequately characterized.

**Data Quality**

Reliability:  
Remarks:

2A  
Reliable with restriction; acceptable, well-documented publication which meets basic scientific principles.

**Reference**

Gehring, P. J., Torkelson, T. R. and Oyen, F. 1967. A Comparison of the Lethality of Chlorinated Pyridines and a Study of the Acute Toxicity of 2-Chloropyridine. *Toxicol. Appl. Pharmacol.* 11, 361-371.

**Other**

## Acute Toxicity – Entry 5 of 5

### Test Substance

Identity: 2-Chloropyridine  
Purity: Not determined  
Remarks: None

### Method

Method: Not stated  
Type: Acute inhalation toxicity  
GLP: No  
Year: 1964  
Species/Strain: Rat  
Sex: Male  
Number of animals/  
sex/dose: 10  
Vehicle: None  
Route of  
administration: Inhalation  
Remarks: Ten male albino rats, weighing 235 to 270 g, were exposed to the test substance via inhalation at a concentration of approximately 6.05 mg/l for 6 hours. The exposure was conducted in a 354 l stainless steel chamber. The total airflow through the system was 49±1 liters/minute. Food and water were available *ad libitum*, except during the period of exposure. During exposure, rats were observed for signs of toxicity and mortality continuously for 1 hour and at ½hour intervals thereafter until the end of the exposure period. After the exposure period, the rats were observed daily for 14 days. A necropsy was performed on all rats.

### Results

Value: LC<sub>50</sub> – < 6.05 mg/l  
Mortality rate: 10/10  
Remarks: All animals died within 3 days after exposure. Observations during exposure included hypoactivity, sedation and ataxia. At the end of 4 hours of exposure, all rats were prostrate. Three rats exhibited dyspnea. Three rats died between 4 and 6 hours of the exposure period. At the end of 6 hours the surviving rats were prostrate, comatose and dyspneic. Within 24 hours, 2 additional rats died. The remaining 5 rats were still prostrate and comatose. Clear ocular discharge was noted.

Within the following 24-hour period after exposure, 4 more rats died. The tenth rat died at 3 days post exposure. Necropsy findings in all rats included congestion of the lungs and liver, slight congestion of the small intestines, blood in the abdominal cavity and /or severe hemorrhages of the stomach, small intestines and urinary bladder.

**Conclusions**

Remarks:

The acute inhalation toxicity has been partially characterized. These data support the data of Gehring et al. (1967).

**Data Quality**

Reliability:

1B

Remarks:

Reliable without restriction; comparable to guideline study.

**Reference**

Wazeter, F. X. 1964. Acute Toxicity Studies in Rats and Rabbits. Report # 122-003. International Research and Development Corporation, Mattawan, MI.

**Other**

## B. Genetic Toxicity In Vitro – Entry 1 of 3

### Test Substance

Identity: 2-Chloropyridine  
Purity: 99%  
Remarks: None

### Method

Method: Ames/*Salmonella* Bacterial Point Mutation Assay  
Type: Reverse mutation assay  
Test system: Bacteria  
GLP: Not stated  
Year: 1987  
Species/Strain: *Salmonella typhimurium*/TA97, TA98, TA100 and TA102  
Metabolic activation: 9000 g (S9) liver homogenate from Arochlor 1254-induced male Sprague-Dawley rats.  
Concentrations tested: 50, 100, 500, 1000 and 5000 µg/plate without S9  
50, 100, 500, 1000, 5000 and 7500 µg/plate with S9  
Statistical methods: Stead et al. (1981) and Bernstein et al. (1982) from the reference list in the cited study.  
Remarks: The test procedures were the same as initially described by Ames et al. (1975) (in reference list of cited study). All assays were conducted in the standard plate incorporation assay on at least 2 separate days both with and without metabolic activation. The test substance was tested at 6 concentrations in duplicate. Appropriate negative (solvent) and positive controls were run in parallel with the assay. The test substance and solvent control were dissolved in dimethyl sulfoxide (DMSO). The test substance was not designated positive or negative unless reproducible results were obtained. A positive response was defined as a reproducible, concentration-related increase in histidine independent revertants over the solvent control concentration in at least one strain/activation combination. A definitive positive or negative result was assigned to a test result when the statistical methods and visual examination of the data agreed. An equivocal response occurred when 1) test results were not reproducible, 2) a low-level, but not concentration-related, increase in *his*+ colonies was obtained or 3) when an increase was observed at only 1 concentration level.

**Results**

Result: 2-Chloropyridine elicited a mutagenic response in all 4 *Salmonella* strains in the presence of the metabolic activation system only. No toxicity was observed at any concentration.

Cytotoxic  
Concentration: None  
Genotoxic effects: Negative without metabolic activation. Positive with metabolic activation in all tester strains.

Statistical results: Not stated  
Remarks: None

**Conclusions**

Remarks: This endpoint has been adequately characterized.

**Data Quality**

Reliability: 1B  
Remarks: Reliable without restriction; comparable to guideline study.

**Reference**

Claxton, L. D., Dearfield, K. L., Spanggord, R. J., Riccio, E. S. and Mortelmans, K. 1987. Comparative mutagenicity of halogenated pyridines in the *Salmonella typhimurium*/mammalian microsome test. *Mutat. Res.* 176, 185-198.

**Other**

## Genetic Toxicity In Vitro– Entry 2 of 3

### Test Substance

Identity: 2-Chloropyridine  
Purity: Not stated  
Remarks: None

### Method

Method: Not stated  
Type: Mammalian cell forward mutation assay  
Test system: Mammalian cells  
GLP: Not stated  
Year: 1992  
Cell type: Heterozygous L5178Y TK<sup>+/−</sup> -3.7.2C mouse lymphoma cells.  
Metabolic activation: S9 homogenate derived from livers of Arochlor-induced rats.  
Concentrations tested: Ranging from 1200-2004 µg/ml without S9 activation.  
Ranging from 400-1100 µg/ml with S9 activation  
Statistical methods: Not stated  
Remarks: Duplicate cultures of L5178/TK<sup>+/−</sup> -3.7.2C cells were treated with or without metabolic activation for 4 hours according to the procedures described by Turner et al. (1984)(in reference list of cited study). The mutagenicity assay was performed according to the procedures described by Doerr et al. (1989) (in reference list of cited study). A positive response was defined as one in which the induced mutant frequency was  $>70 \times 10^{-6}$ , at concentrations yielding  $>10\%$  relative total growth. Equivocal responses were those that gave approximately equal evidence of positive and negative responses. The positive control compounds were ethyl methanesulfonate (without S9) and benzo[a]pyrene (with S9).

### Results

Result: In the absence of metabolic activation, 2-chloropyridine induced small increases in the mutant frequencies. In the presence of the metabolic activation system, the test substance greatly increased the frequency of gene mutations.

The test substance induced both small and large colony tk mutants.

Cytotoxic

Concentration:

None

Genotoxic effects:

Positive

Statistical results:

Not stated

Remarks:

An analysis of the relative small and large colony tk mutant frequencies was not performed because the induced response was not sufficient to allow interpretation of the data. Colony sizing was performed on the positive control cultures. Colony sizing analysis for the positive controls demonstrated the ability to recover and quantitate both classes of tk mutants.

### **Conclusions**

Remarks:

This endpoint has been adequately characterized.

### **Data Quality**

Reliability:

2A

Remarks:

Reliable with restriction; acceptable, well-documented publication which meets basic scientific principles.

### **Reference**

Dearfield, K. L., Harington-Brock, D., Doerr, D. L., Parker, L. and Moore, M. M. 1993. Genotoxicity of three pyridine compounds to L5178Y mouse lymphoma cells. *Mutat. Res.* 301, 57-63.

### **Other**

## Genetic Toxicity In Vitro – Entry 3 of 3

### Test Substance

Identity: 2-Chloropyridine  
Purity: Not stated  
Remarks: None

### Method

Method: Not stated  
Type: Mammalian cell chromosome aberrations and micronuclei  
Test system: Mammalian cells  
GLP: Not stated  
Year: 1992  
Cell type: Heterozygous L5178Y TK<sup>+/+</sup>-3.7.2C mouse lymphoma cells.  
Metabolic activation: S9 homogenate derived from livers of Arochlor-induced rats.  
Concentrations tested: Ranging from 1920-1992 µg/ml without S9 activation.  
Ranging from 500-1100 µg/ml with S9 activation  
Statistical methods: Not stated  
Remarks: Duplicate cultures of L5178/TK<sup>+/+</sup>-3.7.2C cells were treated with or without metabolic activation for 4 hours according to the procedures described by Turner et al. (1984)(in reference list of cited study). The cytogenetic analysis was performed according to the procedures described by Doerr et al. (1989) (in reference list of cited study). For the cytogenetic endpoints a positive call is based upon meeting 2 criteria: The response was double the negative control for not only the experiment but also the periodically updated historic means for negative controls. Positive control cultures were analyzed for cytogenetic endpoints only for those compounds that demonstrated a very weak or equivocal response in the mutagenesis assay. The positive control compound was ethyl methanesulfonate (without S9).

**Results**

Result: In the absence of metabolic activation, the test substance induced a small increase in the frequency of chromosome aberrations. In the presence of metabolic activation, it significantly increased the frequency of chromosome aberrations. The test substance significantly increased the number of micronuclei with and without metabolic activation.

Cytotoxic

Concentration: None

Genotoxic effects: Positive

Statistical results: Not stated

Remarks: An analysis of the relative small and large colony tk mutant frequencies was not performed because the induced response was not sufficient to allow interpretation of the data. Colony sizing was performed on the positive control cultures. Colony sizing analysis for the positive controls demonstrated the ability to recover and quantitate both classes of tk mutants.

**Conclusions**

Remarks: This endpoint has been adequately characterized.

**Data Quality**

Reliability: 2A

Remarks: Reliable with restriction; acceptable, well-documented publication which meets basic scientific principles.

**Reference**

Dearfield, K. L., Harington-Brock, D., Doerr, D. L., Parker, L. and Moore, M. M. 1993. Genotoxicity of three pyridine compounds to L5178Y mouse lymphoma cells. *Mutat. Res.* 301, 57-63.

**Other**

## C. Repeated Dose Toxicity

### Test Substance

Identity: 2-Chloropyridine  
Purity: 99.7%

### Method

Method/guideline followed: OECD TG-407  
Test type: Oral  
GLP: Yes  
Species: Rat  
Strain: Sprague-Dawley (CrI: CD(SD) IGS BR)  
Number and sex: 5 males and 5 females/group. Weight (mean  $\pm$  SD) at the start of the study for males and females was  $203 \pm 4$  g and  $159 \pm 5$  g, respectively.  
  
Route of administration: Oral (gavage). Vehicle – corn oil.  
Duration of test: 28 days  
Dose level: 2, 10 or 45 mg/kg/day at a constant dosing volume of 2 ml/kg.  
  
Exposure period: 28 days  
Frequency of treatment: Once daily 7 days per week  
Control group and treatment: Yes. Control group dosed with vehicle only.  
Post-exposure observation period: None  
Methods: Body weights were recorded twice during the week prior to commencement of dosing and then daily from the start of dosing. Food consumption was measured and recorded twice each week, commencing at least one week prior to the start of treatment until the end of the study. All animals were checked twice/day for viability and daily for general clinical abnormalities and overall condition. Once during the pre-treatment week and weekly thereafter, a more detailed examination was made of all animals. Observations included but were not limited to the following: posture/condition on first approach, ease of removal from cage, body temperature, condition of eyes and coat, presence of salivation, latency, level of mobility, rearing, grooming, urination/defecation, arousal, tremor/convulsions, vocalization, piloerection, palpebral closure, gate abnormalities, and unusual

behavior. Once during the pre-treatment week and during week 4 of treatment, the following additional functional assessments were performed at an approximately standardized time of day: reaction to sudden sound, reaction to touch, grip strength, pain perception, landing foot splay, and motor activity. Blood was collected at necropsy for hematology (hemoglobin concentration, hematocrit, red and white blood cell count, differential white blood cell count, platelet count, red blood cell indices (MCV, MCH, and MCHC), examination of blood smears for cellular morphology (45 mg/kg) and prothrombin time. A portion of the blood was treated with heparin, centrifuged and the plasma was assayed for aspartate aminotransferase, alanine aminotransferase, creatinine, urea nitrogen (BUN), glucose, sodium, potassium, chloride, total protein, albumin, A/G ratio, calcium, phosphate total bilirubin and cholesterol. Urine was assayed for appearance, specific gravity, volume, pH, protein, glucose and ketones. Organ weights were taken for brain, epididymis, heart, liver, lungs, kidneys, adrenal glands, ovaries, pituitary gland, submaxillary salivary gland, prostate, thyroid with parathyroids, testes, spleen, and thymus, and uterus. Weighed tissues plus the following additional tissues from the control and high dose groups were fixed in formalin and examined histopathologically: abnormal tissue, aortic arch, eyes, trachea, esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, mesenteric lymph node, optic nerve, sciatic nerve, pancreas, spinal cord, seminal vesicles, skin and mammary gland, sternum, submandibular lymph node, thigh muscle, vagina, and urinary bladder. Histological examination was also conducted on the livers and kidneys of all intermediate and low dose animals. Mean values were calculated for body weight, feed consumption, organ weights, hematology and clinical chemistry. Body weight, food consumption, neurotoxicity data, hematology, clinical chemistry and selected urinalysis data were statistically analyzed for homogeneity of variance using the 'F-max' test. If the group variances appeared homogeneous, a parametric ANOVA was used and pairwise comparisons made via Student's t-test using

Fisher's F-protected LSD. If the variances were heterogeneous, log or square root transformations were used in an attempt to stabilize the variances. If the variances remained heterogeneous, then a non-parametric test, such as Kruskal-Wallis ANOVA, was used. Organ weights were also analyzed as above and by analysis of covariance (ANCOVA) using terminal kill body weight as covariate. Histological incidence data were analyzed using Fisher's Exact Probability Test.

## Results

NOEL: 2 mg/kg  
Remarks: No mortality occurred during the study. At 45 mg/kg subdued behavior was observed in all animals on the first day of treatment. Piloerection and slow respiration were also noted. The onset of all these signs generally occurred 2 hours after dose administration and remained until the last examination was performed for the day. Clinical observations for neurotoxicity, motor activity, and the detailed functional observational battery revealed no findings to indicate the potential of 2-chloropyridine to produce neurotoxicity. Weight gain was reduced at 45 mg/kg. By the end of the first week of treatment the weight gain at this dose, compared to controls, was 63 % in males and 68% in females. At the end of treatment animals at the top dose showed evidence of recovery in their ability to gain weight. Males achieved 90 % and females 98 % of the weight of the control group. Weight gain at the low and mid doses was similar to the control group in both sexes throughout the treatment period. Hemoglobin concentration was decreased (8 % and 7 % in males and females, respectively) at the top dose. Bilirubin (2.5 x control) and calcium (6 % compared to controls) were increased at the top dose. Total protein, albumin, and cholesterol concentration was increased in both sexes at 45 mg/kg and only in males at 10 mg/kg. Liver weight was increased at the top dose in both sexes (M-43 %; F-68 %) and only in females (27 %) at the mid dose. Histological examination of the liver revealed centrilobular hypertrophy in 1/5 males at the mid dose and 4/5 males and 4/5 females at the top dose.

**Conclusions**

Remarks:

The primary effect of exposure to 2-chloropyridine is the effect on the liver. The findings are consistent with an adaptive response to treatment. The history of weight gain from initial exposure to the end of treatment supports this conclusion. However, the increase in bilirubin, albumin and cholesterol at the top and mid doses may indicate an adverse effect to the liver as these variables are not always present when this organ adapts to an increase in workload. But, based on the histopathological evaluation, any adverse effects to the liver are minor.

**Data Quality**Reliability  
(Klimisch):  
Remarks:

1A

Reliable without restrictions. Guideline study (OECD TG-407).

**Reference:**

Clubb, S. K. and J. R. Sutherland. 2004. Pyridine, 2-Chloro – 4 Week Toxicity Study Including Neurotoxicity Screening in rats with Administration by Gavage. Inveresk Research, Tranent, Scotland. Report Number 23098.

**Other**

## D. Reproductive/Developmental Toxicity

### Test Substance

Identity: 2-Chloropyridine  
Purity: 99.7 %

### Method

Method/guideline followed: OECD TG-421  
Test type: Oral  
GLP: Yes  
Species: Rat  
Strain: Sprague-Dawley (CrI: CD(SD) IGS BR)  
Number and sex: 10 males and 10 females/group. Weight (mean  $\pm$  SD) at the start of the study for males and females was  $293 \pm 7$  g and  $184 \pm 5$  g, respectively.

Route of administration: Oral (gavage). Vehicle – corn oil.  
Duration of test: 53 days  
Dose level: 3, 15, or 60 mg/kg at a constant dose volume of 2 ml/kg/day.  
Exposure period: 53 days. The males were treated for at least 4 weeks, starting 2 weeks prior to mating; treatment of females commenced 2 weeks prior to mating and continued through day 4 of lactation.

Frequency of treatment: Once daily 7 days per week.  
Control group and treatment: Yes. Control group dosed with vehicle only.  
Post-exposure observation period: None  
Methods: Body weights of males were recorded once during the week prior to dosing and once weekly up until day 10 of the study and then daily until termination. Female weights were recorded once during the week prior to dosing and weekly up until day 10 of the study and then daily thereafter through gestation day 0 and on gestation days 7, 14 and 20 and lactation days 1 and 4. Litter and pup weight were measured. Food consumption was measured weekly. Clinical observations were conducted daily. Organ weights were measured for the testes, epididymides and liver. Organs examined histologically were the ovary, testis and epididymis. Mating performance, fertility indices, length of gestation, implantation sites, litter performance and

pup survival indices were measured. Pups were examined for externally visible abnormalities. Body weight and food consumption data were subjected to analysis of variance or the Kruskal-Wallis non-parametric analysis. Organ weight data were analyzed by analysis of variance and analysis of covariance using the terminal bodyweight as the single covariate. Histological data were analyzed by Fisher's Exact Probability test.

## Results

Maternal NOEL:	3 mg/kg
Reproduction/ Developmental Toxicity NOEL for males and females:	15 mg/kg
Remarks:	No mortality occurred during the study. At 60 mg/kg there was a reduction in weight gain in both sexes following the first week of treatment (males – 49 %; females – 67 % of controls). Decreased food consumption was evident at 60 mg/kg following 1 week of treatment. Thereafter consumption was similar to controls except during the first half of gestation and in lactation, in which it was slightly lower. There were no effects of treatment on mating performance, fertility or length of gestation. There was a slight decrease in pup survival at the top dose due mainly to the loss of two litters. Mean litter weight was decreased, although not statistically significantly, but mean pup weight was similar across all treatment groups. There was no difference in structural abnormalities amongst pups in any of the treatment groups. There was a significant increase in agalactic pups at the top dose. There was a statistically significant dose related increase in liver weights both sexes at 15 and 60 mg/kg, but this had no effect on fertility or fetal development.

## Conclusions

Remarks:	Neither fertility nor fetal development was affected by treatment with 2-chloropyridine. Pup survival was decreased at the top dose due in part to poor maternal care from inadequate milk production. A number of pups at the top dose were found to lack milk in the stomach. There was an
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increase in liver weights in both sexes at the mid and top dose. This finding is thought to be associated with an adaptive response from an increase in metabolic work load based on results observed in the 4-week repeated dose toxicity study.

**Data Quality**

Reliability  
(Klimisch):  
Remarks:

1A  
Reliable without restrictions. Guideline study (OECD TG-421).

**Reference:**

Clubb, S. K. and J. R. Sutherland. 2004. Pyridine, 2-Chloro – Reproduction/Developmental Toxicity Screening Test. Inveresk Research, Tranent, Scotland. Report Number 23234.

**Other**