FOREWORD INTRODUCITON

5-Ethyl-2-picoline

CAS N°: 104-90-5

SIDS Initial Assessment Report

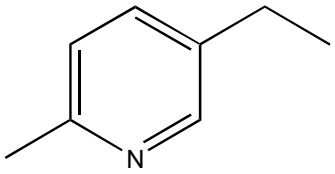
For

SIAM 3

Williamsburg, Virginia, 13-16 February 1995

1. Chemical Name:	5-Ethyl-2-picoline
2. CAS Number:	104-90-5
3. Sponsor Country:	Switzerland National SIDS Contact Point in Sponsor Country: Mr Georg KARLAGANIS-MEYER
4. Shared Partnership with:	
5. Roles/Responsibilities of the Partners:	
• Name of industry sponsor /consortium	
• Process used	
6. Sponsorship History	
• How was the chemical or category brought into the OECD HPV Chemicals Programme ?	
7. Review Process Prior to the SIAM:	SIDS Dossier and Testing Plan were reviewed at SIDS Review Meeting in September 1993, where the following SIDS Testing Plan was agreed: no testing ( ) testing (X) Ecotoxicology : Acute Toxicology to Daphnia Acute Toxicology to Algae Toxicology : Reproductive toxicity
8. Quality check process:	
9. Date of Submission:	14 November 1994
10. Date of last Update:	
11. Comments:	

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	104-90-5
Chemical Name	5-Ethyl-2-picoline
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

This chemical is currently of low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

This chemical was produced in the range of 10,000-50,000 tonnes in 1992. This chemical is mainly used as an industrial intermediate for the production of nicotinic acid and nicotinamide. This chemical may be released to water and air during production and filling processes. In surface water this chemical will degrade and will not bioconcentrate in fish. In air the substance is degraded quite rapidly.

This chemical has a log Pow<3, a relatively high water solubility and is degradable. The lowest aquatic effect concentrations were determined with algae (NOEC(72h): 0.689mg/l). Applying an assessment factor of 10 the resulting PNEC is 0.0689mg/l. This value has to be compared with that derived from the lowest toxicity value of the acute tests (biomass algae: EC50(72h): 30.6mg/l). An assessment factor of 100 has to be chosen when L(E)C50 values for all three taxonomic groups are available. With this assessment factor the PNEC is 0.31mg/l. Comparing the two derived PEC values (0.002mg/l and 0.03mg/l) with the lower PNEC of 0.0689 mg/l gives PEC/PNEC ratios of 0.03 and 0.44. This chemical is of moderate acute toxicity, is not genotoxic, has to be classified as corrosive and has no effect on the general reproductive performance of test animals. Based on the NOEL of 30mg/kg/day from the 28-days oral toxicity study in rats, the estimated dose of low concern (EDLC) can be calculated taking into account an uncertainly factor (UF) of 100, so 0.3 mg/kg/day. EDLC/EHEocc = 37.5.

The results of occupational exposure do not give cause for concern, and no hazard to human health exists for the general population in the vicinity of the plant.

NATURE OF FURTHER WORK RECOMMENDED

FULL SIDS SUMMARY

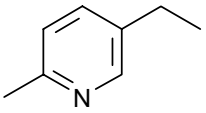
CAS NO: 104-90-5		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point	NA	not specified	-70.9 °C (freezing point)
2.2	Boiling Point	NA	not specified	178.3 °C (at 101.3 kPa)
2.3	Density	NA	not specified	0.9208 g/cm³
2.4	Vapour Pressure	NA	Calculated	0.1853 kPa at 20 °C
2.5	Partition Coefficient (Log Pow)	NA	Calculated	2.27 - 2.52
2.6 A.	Water Solubility	NA	not specified	12'000 mg/l at 20 °C
2.6 B	pKa	NA	not specified	6.6 at 25 °C
ENVIRONMENTAL FATE / BIODEGRADATION				
3.1.1	Photodegradation	NA	Estimated	In air T½ = 6 days
3.1.2	Stability in Water			not available
3.3	Transport and Distribution	NA	Calculated (Fugacity Level 1 Type)	In Air 23.5 % In Water 62.3 % In Soil 13.9 % In Sediment 0.3 % In susp. Sed. 0.01 % In Fish 0.0008 %
3.5	Biodegradation	Act. sewage sludge Act. sewage sludge	OECD 301E OECD 302B	77 % after 28 days 98.7 % after 21 days
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	Salmo gairdneri	OECD 203	55.6 < LC50 (96hr) < 100mg/l NOEC (96hr) < 9.5 mg/l LOEC (96hr) ≤ 9.5 mg/l
		Pimephales promelas	not specified	LC50 (96hr) = 81.1 mg/l
4.2	Acute Toxicity to Aquatic Invertebrates	Daphnia magna	OECD 202	EC50 (24hr) = 83.8 mg/l EC50 (48hr) = 39.6 mg/l
4.3	Toxicity to Aquatic Plants e.g. Algae	Selenastrum capricor-nutum	OECD 201	ErC50 (72hr) = 61.2 mg/l EbC50 (72hr) = 30.6 mg/l NOEC (72hr) = 0.689 mg/l
4.4	Toxicity to Bacteria		UBA LTwS Nr. 10	TTV (18 hr) = 38.8 mg/l

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 104-90-5
Chemical Name: 5-Ethyl-2-picoline (OECD)
Molecular Formula: C8H11N
Structural Formula:



Molecular Weight: 121.18
Synonyms: 5-Ethyl-2-methylpyridine
2-Methyl-5-ethylpyridine
Pyridine, 5-ethyl-2-methyl-
MEP
In this report the synonym MEP will be used

1.2 Purity/Impurities/Additives

Purity: ≥ 96% (w/w)

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

2.1.1. Production

Available data indicate a production volume in the range of 10'000 - 50'000 t in 1992. In Switzerland the production for use as an organic intermediate on site amounted to 14'000 tons.

2.1.2. Manufacturing and Distribution

MEP is manufactured in a dedicated plant by catalytic reaction of paraldehyde and ammonia at a temperature of 230°C and at a pressure of 80-100 bar in a closed system. After work-up and distillation the pure product is stored in tanks, from where it is transferred to the internal user mainly by pipeline. Quantities sold to other chemical manufacturers are supplied in drums or tank cars. Information from other manufacturers in other countries are not available.

2.1.3. Uses

The chemical is mainly used as an industrial intermediate for the production of nicotinic acid and nicotinamide. A small part of the annual production is used either as a solvent in organic synthesis (360 t) or as an intermediate by third parties (40 t). Non-dispersive use.

2.2 Environmental Exposure and Fate

2.2.1 Exposure Relevant Properties

Water solubility: 12 g/l at 20°C

Partition coefficient log Pow: 2.27 - 2.52

Vapour pressure: 1.853 hPa at 20°C

Biodegradation (OECD 301E): 40% after 7 days

46% after 14 days

64% after 21 days

77% after 28 days

MEP is not readily biodegradable due to missing the 10-day window criterion

OECD 302B: 85.7% in 7 days

98.7% after 21 days

2.2.2 Releases from manufacturing

a) Release to air

MEP is produced in one production plant in Switzerland in a closed system. The gaseous releases from the production process are collected and burned in the incineration plant of Lonza (the Swiss manufacturer). No residual MEP is found in the gas after incineration.

The quantity of MEP released into the air from the storage tank amounts to 54.2 g/h. Taking into account the local geographic and climatic conditions, the MEP concentration in the air in the vicinity of the plant can be calculated as

$cair = (rr \cdot t) / (vw \cdot lh \cdot ws \cdot t) = 4.7 \cdot 10^{-5}$ mg/m^3

rr = release rate = 54.2 g/h

t = time interval = 1 h

vw = valley width = 800 m

lh = layer height = 200 m

ws = mean wind speed = 2 m/s

b) Release to water

The amount of MEP which is released from production to one waste water treatment plant is 30 kg/day. In the effluent of the treatment plant, no MEP could be analytically measured (detection limit: 0.3 mg/l).

Under worst case conditions (flow of the receiving water during winter time: 20 m^3/s; MEP concentration in the effluent = detection limit) the Predicted Environmental Concentration PEC in the receiving water (river Rhone) is

$PEC = (caq \cdot wv) / (rf \cdot t) = 0.002$ mg/l

caq = concentration of MEP in the effluent = 0.3 mg/l

wv = effluent volume = 12'000 m^3

rf = flow of river Rhone = 20 m^3/s

t = time interval = 1 day (86'400 s)

This calculation may not be valid for other production sites which are connected to waste water treatment plants located at smaller rivers. In such cases the effluent concentration of 0.3 mg/l gives a MEP concentration of 0.03 mg/l in the receiving water, assuming a dilution factor of 10.

The data show that a high elimination rate of 90% has been achieved.

c) Release to soil

There is no release to soil from the production and filling process.

2.3 Human Exposure

2.3.1 Occupational Exposure

The concentration of MEP in the air was measured in three areas within the production site. The average concentrations were 27, 53, and 59 $\mu g/m^3$.

2.3.2 Consumer Exposure

In Switzerland MEP is mainly used as an intermediate in chemical synthesis, a smaller part is used as a solvent in chemical reactions. In the Swiss product register there are no products containing the substance. Information from other countries are lacking.

3 TOXICITY

3.1 Ecotoxicity

a) Acute toxicity to fish

Rainbow trout (Salmo gairdneri)	55.6 mg/l < LC50 (96h) < 100 mg/l
	NOEC (96h) < 9.5 mg/l
	LOEC (96h) ≤ 9.5 mg/l

The test has been performed under static conditions and a solvent control has been carried out.

Fathead minnow	LC50 (96h): 81.1 mg/l
(Pimephales promelas)	

The test has been performed under flow-through conditions and a solvent control has been carried out.

b) Toxicity to daphnids

Daphnia magna (Immobilisation):	EC50 (24h): 83.8 mg/l
	EC50 (48h): 39.6 mg/l

The test has been performed under static conditions with solvent control.

c) Toxicity to algae

Selenastrum capricornutum	EC50 (72h): 61.2 mg/l (growth)
	EC50 (72h): 30.6 mg/l (biomass)
	NOEC (72h): 0.689 mg/l (growth, biomass)

d) Toxicity to bacteria

Pseudomonas putida Toxicity threshold value: 38.8 mg/l (18h)

3.2 Human Toxicity

a) Acute toxicity

Oral:	LD50: 710 mg/kg (rat)
	LD50: 569 mg/kg (mouse)
	LD50: 459-918 mg/kg (rabbit)
Inhalation:	1000 ppm killed 5 of 6 rats within 4 hours
	LC100 (3.7h): 1700 ppm (rats)
Dermal:	LD50: 1000 mg/kg (rabbits)
	LD50: 2500 mg/kg (guinea pig)

Skin irritation: corrosive

Sensitisation: no data

b) Repeated dose toxicity

Oral (gavage): NOEL = 30 mg/kg/day (rat)

LOEL = 95 mg/kg/day (rat)

No mortality at all dose levels. 300 mg/kg/day: reduced bodyweight gain and food intake; elevated BUN, creatinine, ASAT, increased relative liver and kidney weights. 95 mg/kg/day: slight deviations of clinical chemistry parameters and increased liver weight. Hyaline droplets nephropathy in males at 95 and 300 mg/kg/day.

c) Reproduction/Developmental toxicity

Administration of MEP at levels up to 300 mg/kg/day for 15 days before pairing and throughout the study until termination was without effect on the general reproductive performance of the test animals. The NOEL for general toxicity was considered to be 95 mg/kg/day for males and 30 mg/kg/day for females. For offspring parameters, the NOEL was considered to be 95 mg/kg/day.

d) Genetic toxicity

Bacterial test: Ames test using five strains of S. typhimurium (TA1535, TA1537, TA1538, TA98, TA100)

Negative both with and without metabolic activation

Non-bacterial test in vitro:

MEP was not clastogenic in a chromosome aberration test using human lymphocytes in the presence of metabolic enzymes. Without metabolic activation a clastogenic activity was seen near the toxic concentration. This positive result was not confirmed in two subsequent experiments also using human lymphocytes. It is therefore concluded that the positive response in the first experiment most probably arose by chance and does not represent in vitro genotoxicity.

Non-bacterial test in vivo:

No chromosomal or other damage detected in an oral (gavage) micronucleus test with mice.

e) Other human health related information

No data

3.3 Initial Assessment

3.3.1 Initial Assessment for Human Health

MEP is of moderate acute toxicity, is not genotoxic, has to be classified as corrosive and has no effect on the general reproductive performance of test animals.

Based on the NOEL of 30 mg/kg/day from the 28 day oral toxicity study in rats, the estimated dose of low concern (EDLC) can be calculated taking into account an uncertainty factor (UF) of 100 (according to the OECD provisional guidance for the initial assessment of health effects):

EDLC = (NOEL/UF) = 0.3 mg/kg/day

Occupational

The main exposure route at the workplace will be inhalation. The estimated occupational human exposure (EHEocc) can be calculated based on the maximum average concentration (59 μg/m3) measured at the production site, assuming inhalation of 10 m3 air per working day and a bodyweight of 70 kg.

EHEocc = 10 m^3 · 0.059 mg/m^3 / 70 kg = 0.008 mg/kg/day

EDLC / EHEocc = (0.3 mg/kg/day) / (0.008 mg/kg/day) = 37.5

According to this result occupational exposure does not give cause for concern.

General population

The estimated environmental human exposure for the general population (EHEgp) can be calculated from the estimated air concentration in the vicinity of the plant ($4.7 \cdot 10^{-5}$ mg/m^3):

EHEgp = (30 m^3 · $4.7 \cdot 10^{-5}$ mg/m^3) / 70 kg = $2.0 \cdot 10^{-5}$ mg/kg/day

(Assumed daily respiratory volume for the general population: 30 m^3

Weight of an adult person: 70 kg)

EDLC / EHEgp = (0.3 mg/kg/day) / ($2.0 \cdot 10^{-5}$ mg/kg/day) = 15'000

Conclusion: No hazard to human health exists for the general population in the vicinity of the plant.

Conclusion

MEP is of moderate acute toxicity but corrosive. It is of low subacute toxicity in rats, is not genotoxic and has no effect on the reproductive performance of test animals in a reproduction/developmental toxicity screening test.

3.3.2 Initial Assessment for the Environment

MEP has a rather strong tendency to migrate to the air (24 %) and water (62 %) compartment as indicated by the level I model calculation. Only minor amounts migrate to soil (14 %) and sediment (0.3 %).

MEP may be released to water and air during production and filling processes. MEP is not readily biodegradable, but is expected to meet the criterion for inherent biodegradability. It will not bioconcentrate in fish. In buffered surface waters (pH between 7 and 9) volatilization is expected to be an important elimination pathway. In the air the substance is degraded quite rapidly.

The lowest aquatic effect concentrations were determined with algae (NOEC (72h): 0.689 mg/l). Applying an assessment factor of 10 the resulting PNEC is 0.0689 mg/l. This value has to be compared with that derived from the lowest toxicity value of the acute tests (biomass algae: EC50 (72h): 30.6 mg/l). According to the provisional OECD guidance document for the initial assessment of aquatic effects, an assessment factor of 100 has to be chosen when L(E)C50 values for all three taxonomic groups are available. With this assessment factor the PNEC is 0.31 mg/l.

Comparing the two derived PEC values (0.002 mg/l and 0.03 mg/l) with the lower PNEC of 0.0689 mg/l gives PEC/PNEC ratios of 0.03 and 0.44, respectively. Hence there is no concern for aquatic organisms.

MEP has a log Kow < 3, a relatively high water solubility and is degradable. It would therefore not be expected to bioaccumulate in the environment.

3.3.3 Conclusion

The substance is mainly used as an industrial intermediate for the production of nicotinic acid and nicotinamide. During production and filling it may be released to wastewater and air. In the sewage treatment plant at the production site a high removal rate has been observed. In air the substance will be degraded fairly rapidly.

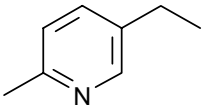
MEP is moderately toxic to aquatic organisms, degradable and is not expected to bioaccumulate.

The environmental hazard assessment showed that MEP does not give cause for concern.

4 RECOMMENDATIONS

5-Ethyl-2-picoline is of low current priority for further work in the SIDS context. No further studies are required to evaluate potential health and environmental effects.

1.0.1. Substance Information

A.CAS-number	104-90-5
B.Name *(IUPAC name)*	5-Ethyl-2-methylpyridine
C.Name *(OECD name)*	5-Ethyl-2-picoline
E.EINECS-Number	203-250-0
F.Molecular Formula	$C_8H_{11}N$
G.Structural Formula	
J. Molecular Weight	121.18

1.0.2. OECD Information

A. Sponsor Country:	Switzerland
B. Lead Organisation:	Federal Office of Environment, Forests and Landscape
Contact Person:	Dr. G. Karlaganis Federal Office of Environment, Forests and Landscape Hallwylstrasse 4 CH - 3003 Berne Tel. +41 31 322 69 55 Fax +41 31 324 79 78
C. Name of Responder:	Dr. F. Camponovo LONZA AG Münchensteinerstrasse 38 CH - 4002 Basel

1.1 General Substance Information

A. Type of Substance	organic
B. Physical State *(at 20°C and 1.013 hPa)*	liquid
C. Purity	≥ 96% (w/w)
1.2 Synonyms	2-Methyl-5-ethylpyridine Pyridine, 5ethyl-2-methyl- MEP
1.3 Impurities	No general information available
1.4 Additives	No general information available

2.1 Melting or decomposition point -70.9°C

Method:	Not specified
GLP:	No data
Remark:	Freezing point
Reference:	[1]

2.2 Boiling point 178.3°C at 1013 hPa

Method	Not specified
GLP	No data
Reference	[2]

2.3 Vapour pressure 1.853 hPa at 20°C

Method	Experimental values determined in the range from 180°C to 50°C. Extrapolation down to 20°C by fitting using the Antoine equation
Reference	[3]

2.4 Partition coefficient

2.4.1 Partition coefficient n-octanol/water log Pow

Value	2.27 - 2.52
Method	Calculated
Reference	[2]
Value	2.39
Method	Calculated with KOWWIN (v1.67) based on SMILES: n(c(ccc1CC)C)c1 CHEM: Pyridine, 5-ethyl-2-methyl- MOL FOR: C8 H11 N1 MOL WT: 121.18
Reference	EPI SUITE v3.12 [27]

2.4.2 Partition coefficient water - air Henry's Constant

Value	1.14E-05 – 1.9 E-05 atm m^3 mol^{-1} 1.14E-05 (bond estimation method) 1.38E-05 (group estimation method) 1.90E-05 (VP/WSol estimation method)
Method	Calculated with HENRYWIN (v3.10) based on SMILES: n(c(ccc1CC)C)c1 CHEM: Pyridine, 5-ethyl-2-methyl- MOL FOR: C8 H11 N1 MOL WT: 121.18 Exp VP: 1.43E+00 mm Hg Exp WSol: 1.2 E+04 mg/l
Conclusion:	The Henry's Law constant indicates that the chemical in the neutral form is expected to volatilize from water surfaces [28]
Reference	EPI SUITE v3.12 [27]

2.4.3 Partition coefficient soil/sediment - water Koc

Value	167
Method	Calculated with PCKOC (v1.66) based on SMILES: n(c(ccc1CC)C)c1 CHEM: Pyridine, 5-ethyl-2-methyl- MOL FOR: C8 H11 N1 MOL WT: 121.18
Conclusion	The Koc value suggests that the chemical is expected to have moderate mobility in

	soil. The pKa of 6.6 indicates that the chemical exist in the protonated form under acidic conditions. Cations adsorb more strongly to soil surfaces than neutral molecules. If released to water, the substance is not expected to adsorb to suspended matter and sediment.
Reference	EPI SUITE v3.12 [27]
2.5 Water solubility	12 g/l at 20°C
Method	Not specified
GLP	No data
Reference	[1]
2.6 pKa value	6.6 at 25°C
Method:	Titration of the hydrochloride
Conclusion:	The chemical is a weak base. A pH value of 8.8 results for a solution with 0.001 mol/l (121 mg/l). This corresponds to a dissociation rate of less than 1 %. The rate of dissociation at different pH values can be calculated as follows ($\alpha = K_b / (K_b + c[OH^-])$ pH 5.0 97.5 % pH 6.0 80.0 % pH 6.6 50.0 % pH 7.0 28.5 % pH 7.4 13.5 % pH 8.0 3.8 %
Reference	[3]
2.7 Flash point (liquids)	70°C (closed cup)
Method	Pensky-Martens DIN 51758
GLP	No
Reference	[3]
2.8 Other data	
Density	0.9208 g/cm^3 at 20°C
Reference	[1]
Ignition temperature	503.9°C
Reference	[4]
Flammable limits in air	1.1% to 6.6%
Reference	[4]

3.1 Production Range 10'000 - 50'000 tons in 1992

3.2 Information concerning Uses Chemical industry: used in synthesis
Remark:
The production for use as organic intermediate on site amounted to 14'000 tons. A small part, amounting to 400 tons, is used as solvent in organic synthesis (90%) or as intermediate (10%) by third parties.
Non dispersive use.

3.3 Options for disposal Burn in a chemical incinerator

4.1 Stability

4.1.1 Photodegradation

Type: Air
Indirect photolysis:
Type of sensitizer: OH radicals
Rate constant: 2.4141 E-12 cm^3/molecule-sec
Degradation: 50% in 53.2 hours (4.4 days)
(12-hr day; 1.5E6 OH/cm3)
Method: Calculated with AOP (v1.91) based on

SMILES: n(c(ccc1CC)C)c1
CHEM: Pyridine, 5-ethyl-2-methyl-
MOL FOR: C8 H11 N1
MOL WT: 121.18
Hydrogen Abstraction = 1.2373 E-12 cm3/molecule-sec
Reaction with N, S and -OH = 0.0000 E-12 cm3/molecule-sec
Addition to Triple Bonds = 0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds = 0.0000 E-12 cm3/molecule-sec
Addition to Aromatic Rings = 1.1768 E-12 cm3/molecule-sec
Addition to Fused Rings = 0.0000 E-12 cm3/molecule-sec
Reference: EPI SUITE v3.12 [27]

Type: Air
Indirect photolysis:
Type of sensitizer: OH radicals
Concentr. of sensitizer: 5E5 OH/cm^3
Rate constant: 2.74 E-12 cm^3/molecule-sec
Degradation: 50% in ≈ 6 days
Method: Calculated
Reference: HSDB database [25]

4.1.2 Stability in Water

5-Ethyl-2-picoline is not expected to undergo hydrolysis in the environment due to the lack of hydrolyzable functional groups [28]

4.2 Transport and Distribution

Theoretical Distribution (Fugacity Calculation)
Media: Air-biota-sediment-soil-water
Method: Fugacity level I
Results:

Distribution	Compartment
23.5 %	Air
62.3 %	Water
13.9 %	Soil solids
0.3 %	Sediment solids
0.01 %	Suspended sediment
0.0008 %	Biota (fish)

Remarks:
Calculation of the theoretical distribution of 5-Ethyl-2-picoline in the environment using the FUGMOD model level I, version 1. All the default values were used.
Reference: FUGMOD, 1992

Volatilization from Water
Media: Air-water
Volatilization: 50% in 1.5 days (river water)
50% in 20 days (lake water)

Method: Calculated with WVOLWIN based on
CHEM: Pyridine, 5-ethyl-2-methyl-
MOL WT: 121.18
Water solubility: 1.2 E4 mg/l
Vapor Pressure: 1.43 mg Hg
Henry's Law Constant: 1.9E-05 atm m^3 mol^{-1}

Conclusion :

Based on the Henry's Law constant, the volatilization half-life of the chemical in neutral form from a model river (1 m deep, flowing 1 m/sec, wind velocity of 5 m/sec) is estimated as 1.5 days. The volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec) is estimated as 20 days.
In well buffered river waters (pH values between 7.1 and 8.9) 5-Ethyl-2-picoline exists mainly in its neutral form and therefore volatilization from waters may be significant.

Reference: EPI SUITE v3.12 [27]

4.3 Biodegradation

A. Test substance: 5-Ethyl-2-picoline, purity 97.4%
Test type: aerobic
Test medium: Activated sludge from the secondary effluent of a domestic waste-water sewage plant; not adapted
Test method: Modified OECD Screening Test (301 E)
GLP: Yes
Test results: DOC-removal
10% after ~2 days
40% after 7 days
46% after 14 days
64% after 21 days
77% after 28 days
Comments: The substance is not readily biodegradable due to missing the 10-day window criterion.
The standard aniline was degraded within
14 days by 93%.
Conc.: 44 mg/l related to test substance.
Temp.: 21.5 - 25°C.
No information about the pH during the test available. According to the test guideline the pH value should be adjusted to pH 7.4. At this pH, the rate of dissociation of the test substance is minor. Due to the relatively high vapour pressure volatilization of 5-Ethyl-2-picoline could have occured.
Reference: [5]

A. Test substance: 5-Ethyl-2-picoline, purity not specified
Test type: aerobic
Test medium: Activated sludge from municipal waste-water sewage plant
Test method: Zahn-Wellens Test (OECD 302B)
GLP: No

Test results:	DOC-removal 13.3 % after 15 minutes 10.3 % after 1 day 26.8 % after 3 days 85.7 % after 7 days 98.7 % after 21 days
Comments:	No information about the pH during the test available. According to the test guideline the pH value should be adjusted to pH 6.5-8.
Reference:	[26]

4.4 Bioaccumulation

Bioconcentration factor BCF

Value	3 - 46
Method	Calculated
Remark:	Based on a water solubility of 12'000 mg/l at 25°C and an estimated log K_{ow} of 2.49, respective bioconcentration factors (log BCF) of 0.49 and 1.66 for 2-methyl-5-ethylpyridine have been calculated using recommended regression-derived equations.
Conclusion	These BCF values indicate that 2-methyl-5-ethylpyridine should not bioconcentrate among aquatic organisms.
Reference	HSDB database [25]

Value	13.8
Method	Calculated with Bcfwin (v2.15) based on SMILES: n(c(ccc1CC)C)c1 CHEM: Pyridine, 5-ethyl-2-methyl- MOL FOR: C8 H11 N1 MOL WT: 121.18 Log Kow: 2.39
Remark:	An equation valid for nonionics has been used to make the BCF estimate [29]: log BCF = 0.77 log Kow - 0.7 + ∑ Fi where ∑ Fi is the summation of all correction factors applicable to a given substance. For MEP no correction factors have been applied.
Conclusion	The BCF suggests the potential for bioconcentration in aquatic organisms is low
Reference	EPI SUITE v3.12 [27]

4.5 Monitoring Data Analyses of the outlet water of the waste water treatment plant, to which the Swiss production site is connected, have revealed concentrations below the detection level of 0.3 mg/l.

5.1 Toxicity to Fish

5.1.1 Results of acute tests

Test substance:	5-Ethyl-2-picoline, purity 97.4%
Test species:	Rainbow trout (Salmo gairdneri)
Test method:	OECD 203, static
GLP:	Yes
Test results:	55.6 mg/l < LC_{50} (96h) < 100 mg/l
	NOEC (96h) < 9.5 mg/l
	LOEC (96h) ≤ 9.5 mg/l
Comments:	14 - 14.5°C, pH 7.8 - 8.2

The analytical results show that the concentration of the test substance in the fish tank water ranged between 84.6% and 92.9% of the target test concentration at the start of the test and between 76.4% and 77.2% after 96 hours.

The logit model could not be used to determine the LC_{50} and to estimate LC_{20} and LC_{80}, since the 0% and 100% mortality rates were at two tested concentrations spaced by a factor of 1.8.

Reference: [6]

Test substance:	5-Ethyl-2-picoline, purity not specified
Test species:	Fathead minnows (Pimephales promelas)
Test method:	Flow-through
GLP:	No data
Test results:	LC_{50} (96h): 81.1 mg/l
Comments:	26.2°C, pH 7.49
	Values based on measured conc.

Nominal conc.: (mg/l)	23	35	54	83	128
mean measured: (mg/l)	29.3	40.0	51.5	70.3	100

Reference: [7]

5.2 Toxicity to Daphnids

Type of test:	Static
Species:	Daphnia magna
Exposure period:	48 hours
Results:	EC_{50} (24h) = 83.8 mg/l
	EC_{50} (48h) = 39.6 mg/l
Analytical monitoring:	Yes
Method:	In accordance with OECD 202 (1984) and EC Methods for Determination of Ecotoxicity, Part C2 (1992)
GLP:	Yes
Test substance:	5-Ethyl-2-picoline, purity: 97%
Remarks:	Temperature: 19.2 - 20.1°C
	Hardness: 198 - 208 mg/l as $CaCO_3$
	pH: 7.7 - 8.6

At the lowest test concentration, 9.24 mg/l, 5% immobility was seen after 48 hours. The lowest measured concentration at which 100% immobilisation occurred was 153 mg/l.

The results of chemical analysis indicated that intended exposure levels were achieved and adequately maintained during the test:

nominal conc. (mg/l):	10	20	40	80	160	320
mean measured conc. after 0h (mg/l):	10.3	20	41.9	84	169.5	346.5
mean measured conc. after 48h (mg/l):	8.3	17.1	34.9	70.5	139	285

Reference: [22]

5.3 Toxicity to Algae

Species:	Selenastrum capricornutum (CCAP No. 278/4)
Endpoint:	Biomass and growth rate
Exposure period:	72 hours
Results:	Growth rate: ErC_{50} (72h) = 61.2 mg/l Biomass: EbC_{50} (72h) = 30.6 mg/l
Analytical monitoring:	Yes
Method:	OECD 201 (1984) Test vessels loosely plugged with non-porous cotton wool
GLP:	Yes
Test substance:	5-Ethyl-2-picoline, purity: 97%
Remarks:	Temperature: 22.6 - 23.9°C; pH 7.9 - 9.0

The intended exposure concentrations were substantially achieved (between 77 and 94% of their nominal values) and adequately maintained during the test (between 80 and 88% of their starting concentrations). The overall geometric mean measured concentrations were 0.689, 2.40, 7.57, 28.1 and 83.0 mg/l (nominal concentrations: 1, 3.2, 10, 32 and 100 mg/l).

Exposure at measured levels of 2.40 mg/l and above resulted in significant reduction in both the specific growth rates and biomass values compared to control cultures ($p < 0.05$). Thus, the NOEC for both growth rate and biomass was 0.689 mg/l.

Reference: [23]

5.4 Toxicity to Other Aquatic Org. No data available

5.5 Toxicity to Bacteria

Test substance:	5-Ethyl-2-picoline, purity 97.4%
Test species:	Pseudomonas putida
Test method:	UBA Guidelines, LTwS Nr. 10, 1979
GLP:	Yes
Test results:	Toxicity threshold value: 38.8 mg/l Exposure period: 18 hrs
Reference:	[8]

5.6 Toxicity to Terrestrial Organisms No data available

5.7 Biological Effects Monitoring No information available

5.8 Biotransformation and Kinetics in Environmental Species No data available

6.1 Acute Toxicity

6.1.1 Acute Oral Toxicity

Test substance:	5-Ethyl-2-picoline, purity not specified
Test species/strain:	Sprague-Dawley rats; strain Crl:CD(WI)BR
Test method:	OECD 401
GLP:	Yes
Test results:	LD_{50} = 1737 mg/kg (all animals) LD_{50} = 1697 mg/kg (males only) LD_{50} = 1797 mg/kg (females only)

Comment:
Deaths occurred within 2 days. No mortality was noted up to 1020 mg/kg. Common symptoms: lethargy and piloerection on dosing day, thereafter ataxia, salivation and lacrimation. Necropsy findings: discolouration of liver, lungs and gastrointestinal tract. The survivors were free of symptoms by day 11.

Reference: [9]

Test substance:	5-Ethyl-2-picoline, purity not specified
Test species/strain:	Rat
Test method:	DOT
GLP:	No
Test results:	LD_{50} = 710 mg/kg

Comment:
Deaths mainly occurred on day 1. No mortality was noted at 250 mg/kg. Symptoms: lethargy, lacrimation, chromodacryorrhea and tachypnea. No necropsy performed. The survivors were free of symptoms by day 7.

Reference: [10]

Test substance:	5-Ethyl-2-picoline, purity not specified
Test species/strain:	Mouse, Taylors original strain
Test method:	Almost consistent with OECD 401
GLP:	No
Test results:	LD_{50} = 569 mg/kg

Comment:
Deaths occurred on day 1. No mortality was noted at 183 mg/kg. Symptoms: general loss of activity. The survivors were free of symptoms after 24 hours. No necropsy performed.

Reference: [11]

Test substance:	5-Ethyl-2-picoline, purity not specified
Test species/strain:	Female Wistar rats
Test method:	Range-finding study
GLP:	No
Test results:	LD_{50} = 918 - 2295 mg/kg

Comment:
Deaths were noted on day 1. Symptoms: general loss of activity. The survivors were free of symptoms after 24 hours. No necropsy performed.

Reference: [11]

Test substance: 5-Ethyl-2-picoline, purity not specified
Test species/strain: New Zealand White rabbit
Test method: range-finding study
GLP: No
Test results: LD_{50} = 459 - 918 mg/kg
Comment:
Deaths were noted on day 1. Symptoms: general loss of activity. The survivors were free of symptoms after 24 hours. No necropsy performed.
Reference: [11]

6.1.2 Acute Inhalation Toxicity

Test substance: 5-Ethyl-2-picoline, purity not specified
Test species/strain: Rat
Test method: No details given
GLP: Not stated
Exposure time: 4 hours
Comment: After 4 hours exposure at 1000 ppm 5 of 6 animals died.
Reference: [12]

Test substance: 5-Ethyl-2-picoline, purity not specified
Test species/strain: Rat
Test method: No details given
GLP: Not stated
Test results: LC_{100} 3.7 hrs = 1700 ppm
Reference: [13]

6.1.3 Acute Dermal Toxicity

Test substance: 5-Ethyl-2-picoline, purity not specified
Test species/strain: Rabbit
Test method: No details given
GLP: Not stated
Test results: LD_{50} = 1000 mg/kg
Reference: [14]

Test substance: 5-Ethyl-2-picoline, purity not specified
Test species/strain: Guinea pig
Test method: No details given
GLP: Not stated
Test results: LD_{50} = 2500 mg/kg
Reference: [14]

6.2 Corrosiveness/Irritation

6.2.1 Skin Irritation

Test substance: 5-Ethyl-2-picoline, purity ≥ 96%
Test species/strain: New Zealand White rabbit
Test method: OECD 404
GLP: Yes
Test results:
The test substance was applied for 4 hours under occlusion to the intact skin of rabbits. One hour after removal of the wrapping a

black discolouration was noted at all test sites. On day 1 the test sites were covered by black, semi-hard or hard indented skin. The skin surrounding the test sites reacted with slight to moderate edema and moderate to severe erythema. This irritation completely regressed and was not noted on the 14 day observation. The substance was classified as corrosive (causes burns) to rabbit skin according to the EEC Commission Directive 67/548/EEC.
Reference: [15]

6.2.2 Eye Irritation

Test not necessary because of skin corrosion.

6.3 Skin Sensitisation No data available

6.4 Repeated Dose Toxicity

Test substance: 5-Ethyl-2-picoline, purity 97.8%
Test species/strain: Sprague-Dawley rat (males and females)
Test method: OECD 407
GLP: Yes
Test description: route of administration: gavage
exposure period: 28 days
frequency of treatment: daily
post exposure observation period: none
doses: 30, 95, 300 mg/kg day
control group: yes
Test results: NOEL = 30 mg/kg bw d
LOEL = 95 mg/kg bw d
Comment:
No mortality at all dose levels.
300 mg/kg/day: reduced body-weight gain and food intake; elevated BUN, creatinine, ASAT, increased relative liver and kidney weights.
95 mg/kg/day: slight deviations of clinical chemistry parameters and increased liver weight. Hyaline droplets nephropathy in males at 95 and 300 mg/kg/day.
Reference: [16]

Test substance: 5-Ethyl-2-picoline, purity 97.8%
Test species/strain: Sprague-Dawley rat (males and females)
Test method: Range-finding study
GLP: Not stated
Test description: route of administration: gavage
exposure period: 11 days
frequency of treatment: daily
post exposure observation period: none
doses: 100, 200, 400, 600, 800 and 1200 mg/kg/day
control group: yes
Test results: NOEL = 100 mg/kg bw d
LOEL = 200 mg/kg/bw d
Comment:
All animals at 1200 mg/kg/day died within 3 hours; at 400 and 800 mg/kg/day deaths occurred after 6 or more days. Clinical symptoms: inactivity, labored respiration, roaring, salivation, incoordination, abdominal position. Reduced body weight gain.
Reference: [17]

6.5 Genetic Toxicity

6.5.1 Bacterial Test

Test substance:	5-Ethyl-2-picoline, purity ≥ 96%
Test species/strain:	Salmonella typhimurium TA1535, TA1537, TA1538, TA98, TA100
Test method:	OECD 471
GLP:	Yes
Test results:	Negative
Genotoxic effects:	

	+	?	-
with metabolic activation:	[ ]	[ ]	[x]
without metabolic activation:	[ ]	[ ]	[x]

Comment:	Conc.: 100, 333, 1000, 3330, 5000 µg/plate
Reference:	[18]

6.5.2 Non-bacterial in vitro Test

Test substance:	5-Ethyl-2-picoline, purity ≥ 96%
Test method:	OECD 473 Chromosome aberrations in cultured human lymphocytes
GLP:	Yes
Test results:	Negative
Genotoxic effects:	

	+	?	-
without metabolic activation:	[ ]	[ ]	[x]

Comment:	Conc.: 100, 200, 300, 400 µg/ml Mitotic index reduced by 81% at the highest concentration
Reference:	[19]

Test substance:	5-Ethyl-2-picoline, purity 99.4%
Test method:	OECD 473 Chromosome aberrations in cultured human lymphocytes
GLP:	Yes
Test results:	Negative
Genotoxic effects:	

	+	?	-
without metabolic activation:	[ ]	[ ]	[x]

Comment:	Conc.: 100, 200, 300, 400 µg/ml Mitotic index reduced by 79% at the highest concentration
Reference:	[19]

Test substance:	5-Ethyl-2-picoline, purity 97.8%
Test method:	OECD 473 Chromosome aberrations in cultured human lymphocytes
GLP:	Yes
Test results:	Positive
Genotoxic effects:	

	+	?	-
with metabolic activation:	[ ]	[ ]	[x]
without metabolic activation:	[x]	[ ]	[ ]

Comment:
Conc.: 78.13, 156.25, 312.5, 625, 1250, 2500, 5000 µg/ml
Not clastogenic with metabolic activation; clastogenic at near toxic doses without metabolic activation.
Reference: [20]

6.5.3 Non-bacterial Test in vivo

Test substance: 5-Ethyl-2-picoline, purity 97.6%
Test species/strain: Mouse, CD-1 strain (males and females)
Test method: OECD 474
Micronucleus assay
GLP: Yes
Test results: Negative
Comment:
route of administration: gavage
exposure period: single dose; examinations after 24, 48, 72 h
doses: 156.3, 312.5, 625 mg/kg

No chromosomal or other damage leading to micronucleus formation.
Reference: [21]

6.6 Carcinogenicity No data available

6.7 Toxicity to Reproduction

Type: One-generation study
Species/strain: Sprague Dawley rats, CD strain
Sex: Male/Female
Route of administration: Oral (gavage)
Exposure period: 15 days before pairing, during mating, gestation and lactation until day 4 *post partum*
Frequency of treatment: Daily at a volume-dosage of 10 ml/kg
Premating exposure period: male: 15 days female: 15 days
Duration of the test: 7 weeks
Doses: 30, 95 and 300 mg/kg/day
Control group: Yes
Control animals received the vehicle, 35% aqueous propylene glycol, throughout the same period
Result: No effect on the general reproductive performance of the animals up to 300 mg/kg/day.
NOEL Parental: male: 95 mg/kg/day
female: 30 mg/kg/day
NOEL F1 Offspring: 95 mg/kg/day
Comment:
Animals in all treated groups showed increased salivation after dosing which was most marked at 95 and 300 mg/kg/day. Animals receiving 300 mg/kg/day also showed an apparent reduction in body temperature and abnormal respiration during weeks 2 to 4 after dosing. In addition to these, a small number of other signs were seen infrequently at 300 mg/kg/day. Two males receiving 300 mg/kg/day were killed *in extremis* after dosing with signs including ataxia, partially closed eyes, prostrate posture and underactivity. Terminal investigations revealed reduced/dehydrated gastro-intestinal contents, accentuated

lobular liver patterns, apparently reduced testes, epididymides, prostate glands and seminal vesicles and a small mass on one epididymides. Examination of the masses revealed the presence of spermatozoal granuloma. The deaths were considered to be related to treatment with the test substance.

Bodyweights of males receiving 30 and 95 mg/kg/day were essentially similar to the controls. Males receiving 300 mg/kg/day showed poor bodyweight gains throughout treatment. Female bodyweights before pairing were unaffected by treatment. During gestation bodyweight performance of females receiving 95 and 300 mg/kg/day were reduced. At 300 mg/kg/day the bodyweights during lactation were inferior to those of the controls. Females receiving 30 mg/kg/day were unaffected by treatment with the test substance.

During lactation, females receiving 300 mg/kg/day showed slightly lower food consumption. Food consumption for males and females before pairing and during gestation was unaffected by treatment.

Oestrous cycles were essentially unaffected by treatment. One pair of animals receiving 300 mg/kg/day failed to mate. All other animals mated at the first oestrus and all females were pregnant.

Gestation length for all females was within the normal range of 22-23.5 days.

One female receiving 30 mg/kg/day and three receiving 300 mg/kg/day were terminated as a result of a total litter loss. All females had inactive mammary tissue. Two of the females receiving 300 mg/kg/day showed liver changes a small spleen and pale areas in the kidneys.

Numbers of implantations, survival and growth *in utero*, litter size, offspring viability indices, sex ratio and bodyweight at day 1 of age and weight gain to day 4 were unaffected by maternal treatment at 30 and 95 mg/kg/day.

At 300 mg/kg/day reduced offspring bodyweights were apparent at day 1 when compared with the controls. Subsequent bodyweight gains to day 4 were poor and were associated with a decrease in viability of these offspring. All other offspring parameters were unaffected by treatment at 300 mg/kg/day.

Necropsy of offspring revealed no changes that could be attributed to maternal treatment with the test substance.

No macroscopic or microscopic changes were observed at necropsy of the parental males and females that were considered to be related to treatment. Variations in absolute and bodyweight-relative organ weights were apparent in animals receiving 300 mg/kg/day and were considered to be associated with their reduced bodyweight performance.

Method:	In accordance with draft OECD Guideline 421 (January 1993)
GLP:	Yes
Test substance:	5-Ethyl-2-picoline, purity: 97%
Reference:	[24]

6.7.2 Teratogenicity — No data available

6.8 Specific Toxicities — No data available

6.9 Toxicodynamics, Toxico-Kinetics No data available

6.10 Experience with Human Exposure

No data available

Labelling (provisionally by manufacturer/importer)
Symbol C
R phrases 22-34
S phrases 26-28-36/39

Classification (provisionally by manufacturer/importer)
Class of danger: corrosive
R phrases 22-34

C: Corrosive

R22: Harmful if swallowed
R34: Causes burns

S26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
S28 After contact with skin, wash immediately with plenty of ...
S36/39: Wear suitable protective clothing and eye/face protection

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