FOREWORD INTRODUCTION

P-PHENETIDINE

CASN°: 156-43-4

Substance

End Point	:	**IDENTIFIERS, PHYSICAL AND CHEMICAL PROPERTIES**
Chemical Name	:	**Benzenamine, 4-ethoxy-**
Common Name	:	**p-Phenetidine**
CAS Number	:	**156-43-4**
RTECS Number	:	**SI6465500**

Synonyms

p-Aminophenetole
4-Aminophenetole
p-Ethoxyaniline
4-Ethoxyaniline
4-Ethoxybenzenamine
4-Ethoxyphenylamine
p-Phenetidin
4-Phenetidine

Properties & Definitions

Molecular Formula	:	**C8H11NO**
Molecular Weight	:	**137.18**
Melting Point	:	**ca. 3C**
Boiling Point	:	**253-255C**
State	:	**Solid**
Density	:	**1.065 at 16C**
Vapour Pressure	:	**1.9E-6 kPa(1.4E-8 mmHg) at 25C**
Octanol/Water Partition Coefficient	:	**log Pow = 1.28 at 25C experimental**
Water Solubility	:	**21 g/L at 25 C**
Solubility in other Solvents	:	**Soluble in alcohol**
Colour	:	**Colourless**
General Comments	:	Stable, non-volatile. Becomes red to brown on exposure to air and light. Keep well closed and protected from light.

Overall Evaluation

NEEDS FURTHER WORK

SIDS INITIAL ASSESSMENT

4-Ethoxybenzenamine is non-volatile stable solid, and the production volume is 250-500 tonnes/year, and import level is 20-79 tonnes/year for 1990-1993, respectively in Japan. Also, Japan exported ca. 130-200 tonnes/year for 1990-1993 to other countries. This chemical is stable in neutral, acidic or alkaline solutions, and is classified as "not readily biodegradable" and "low bioaccumulation potential".
The fact that the chemical is moderately toxic to daphnids and algae, but non-toxic to fish, implies the environmental risk presumably to be low.
The PEC is lower than the MTC.

The chemical showed genotoxic effects in bacterial tests, non-bacterial test in vitro and micronucleus test, and NOAEL for repeated dose toxicity was 10 mg/kg/day and NOAEL for reproductive toxicity was 50 mg/kg/day. Daily intake of the chemical was estimated as 8.11E-5 mg/day from calculation using MNSEM 145I exposure model.

In conclusion, 4-ethoxybenzenamine is persistent and toxicological and ecotoxicological tests showed strong and moderate toxicities, respectively. Based on the genotoxicity of the chemical, we concluded that further work should be considered.

ENVIRONMENTAL EXPOSURE

Biodegradability: "not readily biodegradable"

ESTIMATION OF ENVIRONMENTAL FATE, PATHWAY AND CONCENTRATION

Comparison of calculated environmental concentration using several models:

MNSEM Model:
Air: 1.14E-11 ug/L; Water: 0.0362 ug/L; Soil: 9.02E-3 ug/kg; Sediment: 0.286 ug/kg
CHEMCAN2 Model:
Air: 2.78E-11 ug/L; Water: 0.0362 ug/L; Soil: 2.75E-6 ug/kg; Sediment: 0.0397 ug/kg
CHEMFRAN Model:
Air: 5.58E-13 ug/L; Water: 3.62E-3 ug/L; Soil: 1.36E-7 ug/kg; Sediment: 0.0397 ug/kg
UKMODEL Model:
Air: 1.71E-10 ug/L; Water: 0.0363 ug/L; Soil: 0.115 ug/kg; Sediment: 0.230 ug/kg

CONSUMER EXPOSURE

This chemical is mainly used as intermediate for several materials. There are no actual use of this substance itself, and there are no emission and no exposure to consumer.

OCCUPATIONAL EXPOSURE

Production process are done through the closed system operation, and distillation residue is burned in an incinerator. So, there are no emission and no exposure to workers. However, no data on work place monitoring have been reported.

CONCLUSION

In conclusion, 4-ethoxybenzenamine is persistent and toxicological tests showed high toxicity. In toxicology tests, the chemical showed genotoxic effects in bacterial test, non-bacterial test in vitro and micronucleus test. In the case of applying the OECD Provisional Guidance for Initial Hazard Assessment of Full SIDS, this chemical have to perform risk reduction. However, this chemical is used mainly as intermediate for several materials in closed system. Therefore, although exposure to general population through environment may be low, occupational risk should be considered from its genotoxic properties.

RECOMMENDATION

Monitoring and risk reduction in work place of the production site are recommended, from its toxicological properties, according to the OECD provisional guidance for IHA (Initial Hazard Assessment). Also, continuous international information gathering on exposure is recommended as further work.

Production-Trade

Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Geographic Area : **JPN**

Production

Quantity	*Year*
534 t - P	**1990**
200 t - EX	**1990**
520 t - P	**1991**
42 t - EX	**1991**
458 t - P	**1992**
177 t - EX	**1992**
298 t - P	**1993**
58 t - EX	**1993**

General Comments : The following quantities include both production and imports: 534 tonnes for 1990, 520 tonnes for 1991 and 298 tonne for 1993.

References

SIDSP*
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Processes

Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**

Process

Process comments : Production is accomplished by hydrogenation of p-ethoxynitrobenzene. Crude p-phenetidine obtained from such hydrogenation is subjected to distillation to obtain a high degree of purity. Above production is done through the closed system operation. Distillation residue is burned in an incinerator. Therefore no emissions take place in the production process.

References

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Uses

Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Geographic Area : **JPN**

Use

Quantity	*Year*	*Comments*
		This chemical is used as an intermediate for production of the following materials: 75% for food additives. 15% for dyestuffs and pigments. 5% for pharmaceuticals. 5% for other uses.

References

Secondary References : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Uses

Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Geographic Area : **SWE**

Use

Quantity	*Year*	*Comments*
		The substance is used only as a laboratory chemical for very limited and specific purposes.

References

Secondary References : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point	:	**CONCENTRATION**
Chemical Name	:	**Benzenamine, 4-ethoxy-**
CAS Number	:	**156-43-4**
Study type	:	**FIELD**
Geographic Area	:	**JPN**

Test Subject

Organism	*Medium*	*Specification*	*Lifestage*	*Sex*
	AQ	**SURF**		
	SOIL			
	SED			

Test Results

Matrix	*Concentrations*	*Spec.*	*Date*

0 ug/L
In surface water: not detected in 2 areas in Japan, 1977. Detection limit: 1-5 ug/L.

0 ug/L
In surface water: not detected in 11 areas in Japan, 1985. Detection limit: 0.05 ug/L.

0 ug/g
In soil/sediment: not detected in 2 areas in Japan, 1977. Detection limit: 0.5 - 1 ug/g.

0 ug/g
In soil/sediment: not detected in 11 areas in Japan, 1985. Detection limit: 0.005 ug/g.

References

Primary Reference :

#MOREA*
Environmental Monitoring of Chemicals, Environmental Survey Report (Office of Health Studies, Department of Environmental Health), Japan

Secondary Reference :

!SIDSP*
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point	:	**CONCENTRATION**
Chemical Name	:	**Benzenamine, 4-ethoxy-**
CAS Number	:	**156-43-4**
Geographic Area	:	**JPN**

Test Subject

Organism	*Medium*	*Specification*	*Lifestage*	*Sex*
	AIR			
	AQ			
	SOIL			

Test Method and Conditions

Test method description : Multi-Phase Non-Steady State Equilibrium Model for Evaluation of Fate of Chemicals in Environment consisting of Air, Water, Soil and Sediment phases. Version 1.4.5I also called MNSEM 145I method. (Presented by Kikuo Yoshida).

Test Results

Matrix	*Concentrations*	*Spec.*	*Date*
	1.14E-14 mg/L		

In air, also reported as 2.04E-12 ppm. Steady state mass = 2.29E-2 g

3.62E-5 mg/L

In water. Steady state mass = 7.24E+5 g

9.20E-6 mg/kg

In soil. Steady state mass = 1.47E+4 g

2.86E-4 mg/kg

In sediment. Steady state mass = 2.86E+4 g

General Comments : All above given values are calculated values using MNSEM 145I method.

References

Primary Reference : **#URMEA***

Unpublished Report on Exposure Estimation Test conducted by MITI and Environmental Agency, Japan

Secondary Reference : **!SIDSP***

OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **CONCENTRATION**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Geographic Area : **JPN**

Test Subject

Organism	*Medium*	*Specification*	*Lifestage*	*Sex*
	FOOD - PLANT			

Test Results

Matrix	*Concentrations*	*Spec.*	*Date*
In meat.	**2.44E-10 mg/L**		
In milk.	**2.07E-10 mg/L**		
In vegetation.	**1.58E-5 mg/L**		

General Comments : All above given values are calculated using MNSEM 145I method.

References

Primary Reference : **#URMEA***
Unpublished Report on Exposure Estimation Test conducted by MITI and Environmental Agency, Japan

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point	:	**HUMAN INTAKE AND EXPOSURE**
Chemical Name	:	**Benzenamine, 4-ethoxy-**
CAS Number	:	**156-43-4**
Geographic Area	:	**JPN**

Test Subject

Organism	*Medium*	*Specification*	*Route*	*Lifestage*	*Sex*
	AIR				
	WATER				
	FOOD				

Test Method and Conditions

Test method description : Multi-Phase Non-Steady State Equilibrium Model for Evaluation of Fate of Chemicals in Environment consisting of Air, Water, Soil and Sediment Phases, Version 1.4.5.I (also called MNSEM 145I). (Presented by Kikuo Yoshida).

Test Results

Intake	*Spec.*	*Date*
1.73E-10 mg/d Through inhalation of air		
7.24E-5 mg/d Through drinking water		
2.78E-6 mg/d Through ingestion of fish		
1.81E-11 mg/d Through ingestion of meat		
2.53E-11 mg/d Through ingestion of milk		
5.91E-6 mg/d Through ingestion of vegetables and fruits		
8.11E-5 mg/d Total exposure		

General Comments : Above given values are calculated values using MNSEM 145I method.

References

Primary Reference : **#URMEA***
Unpublished Report on Exposure Estimation Test conducted by MITI and Environmental Agency, Japan

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point	:	**BIODEGRADATION**
Chemical Name	:	**Benzenamine, 4-ethoxy-**
CAS Number	:	**156-43-4**
Study type	:	**LAB**
Species/strain/system	:	Standard activated sludge 30 mg/L as suspended solid

Test Substance

Purity Grade	:	**99.78**

Test Method and Conditions

Test method description	:	OECD Guideline 301C. The sludge samples were mixed by stirring in a single container, then cultured at 25C for 1 month. GLP: Yes
Temperature	:	**25 C**
(An)aerobic	:	**AEROB**

Exposure

Exposure Period	:	**1 mo**
Dose / Concentration	:	**100 mg/L**

Test Results

Quantity		*Time*	*Comments on result*
0 %	AV		Degree of biodegradation from BOD28
3 %	AV		Degree of biodegradation from HPLC

General Comments : Above results indicate that the substance should be classified as "not readily biodegradable".

References

Primary Reference : **#MCIBD***
Unpublished Report on Biodegradation Test of (specific chemical) conducted by MITI

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point	:	**PHOTODEGRADATION**
Chemical Name	:	**Benzenamine, 4-ethoxy-**
CAS Number	:	**156-43-4**

Test Substance

Purity Grade	:	**99.0%**

Test Method and Conditions

Test method description	:	Handbook of Chemical Properties Estimation Methods, McGraw Hill Book co., 1981. Depth in the water body estimated 500m. Conversion constant: 6.023E+20. Quantum yield for disappearance of chemicals under solar irradiation: 0.01. GLP: no

Exposure

Dose / Concentration	:	**6.86E-3 mg/L**

Test Results

Quantity		*Time*	*Comments on result*
50 %	LOSS	**22 d**	Estimated half-life.

General Comments	:	The above values are calculated values. Photochemical degradation rate = 1.86E-11 mol/L/s.

References

Primary Reference	:	**#MCITH*** Unpublished Report on Hydrolysis and Photodegradation Test of (specific chemical), HPV/SIDS test conducted by MITI
Secondary Reference	:	**!SIDSP*** OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point	:	**HYDROLYSIS**
Chemical Name	:	**Benzenamine, 4-ethoxy-**
CAS Number	:	**156-43-4**
Study type	:	**LAB**

Test Substance

Purity Grade	:	**99.0%**

Test Method and Conditions

Test method description	:	OECD Guideline 111. Hydrolysis as a function to pH. GLP: yes
Temperature	:	**25 C**

Test Results

Quantity		*Time*	*Comments on result*
50 %	LOSS	**>1 y**	Measured half-life in pH 4.0, 7.0 and 9.0 at 25C.

General Comments	:	Substance is hydrolytically stable.

References

Primary Reference	:	**#MCITH*** Unpublished Report on Hydrolysis and Photodegradation Test of (specific chemical), HPV/SIDS test conducted by MITI
Secondary Reference	:	**!SIDSP*** OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point	:	**BIOCONCENTRATION**
Chemical Name	:	**Benzenamine, 4-ethoxy-**
CAS Number	:	**156-43-4**
Study type	:	**LAB**

Test Substance

Purity Grade	:	**99.8%**

Test Method and Conditions

Test method description	:	OECD Guideline 305C. A flow-through test. GLP: no

Exposure

Exposure Period	:	**6 wk**

Test Results

Organ	*Bioconcent. Factor*	*Calc Basis*	*Time*	*State*	*Comments on result*
	<0		**6 wk**		Log BCF, level 1 exposure
	<1		**6 wk**		Level 2 exposure

References

Primary Reference :

#MCIBD*

Unpublished Report on Biodegradation Test of (specific chemical) conducted by MITI

Secondary Reference :

!SIDSP*

OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **MAMMALIAN ACUTE TOXICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**

Species/strain/system : Rat, strain not specified

Test Results

Organism	*Medium*	*Spec.*	*Route*	*Lifestage*	*Sex*	*Effect*	*Effect Comments*
RAT			**ORL**	**ADULT**	**M F**	**LD50**	Oral LD50 for rats was established as 580 mg/kg.

References

Primary Reference : **RTECS***
Registry of Toxic Effects of Chemical Substances

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **MAMMALIAN ACUTE TOXICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**

Species/strain/system : Mouse, strain not specified

Test Results

Organism	*Medium*	*Spec.*	*Route*	*Lifestage*	*Sex*	*Effect*	*Effect Comments*
MOUSE			**ORL**	**ADULT**	**M F**	**LD50**	Oral LD50 for mice was established as 530 mg/kg.

References

Primary Reference : **RTECS***
Registry of Toxic Effects of Chemical Substances

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **MAMMALIAN ACUTE TOXICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**

Species/strain/system : Rabbit, strain not specified

Test Results

Organism	*Medium*	*Spec.*	*Route*	*Lifestage*	*Sex*	*Effect*	*Effect Comments*
RBT			**ORL**	**ADULT**	**F M**	**LD50**	Oral LD50 for rabbits was established as 7000 mg/kg, under the test conditions.

References

Primary Reference : **JJPAAZ**
Japanese Journal of Pharmacology, 52, 215, (1956)

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **MAMMALIAN ACUTE TOXICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**

Species/strain/system : Rat, strain not specified

Test Results

Organism	*Medium*	*Spec.*	*Route*	*Lifestage*	*Sex*	*Effect*	*Effect Comments*
RAT			**IHL**	**ADULT**		**LC50**	Inhalation LCLO was established as 250 mg/m3 under the test conditions.

References

Primary Reference : **RTECS***
Registry of Toxic Effects of Chemical Substances

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **MAMMALIAN TOXICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	Medium	Specification	Route	Lifestage	Sex	Number exposed	Number controls
RAT			**ORL**	**ADULT**	**M**	**5/GROUP**	**5**
					F	**5/GROUP**	**5**

Species/strain/system : Rat, Crj: F344

Test Substance

Purity Grade : **99.36**
Vehicle - Solvent : Olive oil

Test Method and Conditions

Test method description : Japanese Guideline for 28-Days Repeated Dose Toxicity Testing of Chemicals. GLP: no

Exposure

Exposure Type : **SHORT**
Exposure Period : **42 d**
Dose / Concentration : **10-160 mg/kg/ day**
Exposure comments : Doses of 0, 10, 40, 160 mg/kg/day were given in oral gavage for 42 days.

Test Results

Organ	Effect	Rev.	OnSet	Sex	Affected in Exposed - Controls
BLOOD	**CHNG**				

Decreased number of erythrocytes with increased number of reticulocytes were observed in the 40 and 160 mg/kg/day dose groups of both sexes.

BLOOD BIOCH

Methemoglobinemia occurred in the 160 mg/kg/day dose group.

URINE BIOCH

Increase in the levels of urinary urobilinogen was observed in the 40 and 160 mg/kg/day groups of both sexes.

SPLN SIZE

Increase in spleen weight was noted in the 40 and 160 mg/kg/ day groups.

SPLN CHNG

Congestion of the spleen, increased extramedullary hematopoiesis and hemosiderosis were observed in the 40 and 160 mg/kg/day groups of both sexes.

BONEM STRUC

Myeloid hyperplasia was observed in the 40 and 160 mg/kg/day groups of both sexes.

NOAEL

No adverse effects level was established as 10 mg/kg/day.

References

Primary Reference : **NEZAAQ**
Sato, M. et al. Nippon Eiseigaku Zasshi (Japanese Journal of Hygiene), 109, 42-48, (1991)

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **MUTAGENICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	*Medium*	*Specification*	*Route*	*Lifestage*	*Sex*	*Number exposed*	*Number controls*
BACT			**VTR**				

Species/strain/system : Salmonella typhimurium TA98, TA100

Test Substance

Purity Grade : **<98%**

Test Method and Conditions

Test method description : Preincubation Assay (NTP); with and without metabolic activation. GLP: No

Test Results

Organ	*Effect*	*Rev.*	*OnSet*	*Sex*	*Affected in Exposed - Controls*
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	INC				

The test substance was positive for mutagenicity effect in the strain TA100 cultures with metabolic activation. Questionable results were obtained in cultures without metabolic activation in the same strain, under the test conditions.

Questionable mutagenic effects were obtained in the strain TA98 with metabolic activation and negative without metabolic activation.

References

Primary Reference : **ENMUDM**
Zeiger, E. et al. Environmental Mutagenesis, 9(9), 1, (1980)

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **MUTAGENICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	*Medium*	*Specification*	*Route*	*Lifestage*	*Sex*	*Number exposed*	*Number controls*
BACT			**VTR**				

Species/strain/system : Salmonella typhimurium TA100

Test Method and Conditions

Test method description : Preincubation Assay; with and without metabolic activation. GLP: No

Test Results

Organ	*Effect*	*Rev.*	*OnSet*	*Sex*	*Affected in Exposed - Controls*
	MUT				

The test substance was positive for mutagenic effects in cultures with metabolic activation.

	NEF				

And negative without metabolic activation.

References

Primary Reference : **CPBTAL**
Nohmi, T. et al. Chemical and Pharmaceutical Bulletin (Tokyo), 33, 2877, (1985)

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **MUTAGENICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	*Medium*	*Specification*	*Route*	*Lifestage*	*Sex*	*Number exposed*	*Number controls*
HAMST			**VTR**				

Species/strain/system : Chinese hamster CHL cells

Test Substance

Purity Grade : **99.9%**
Vehicle - Solvent : DMSO

Test Method and Conditions

Test method description : Japanese Guideline for Screening Mutagenicity Testing of Chemicals. GLP: No

Exposure

Exposure comments : Positive control: - S9: mitomycin C. + S9: cyclophosphamide. Doses for -S9: 0, 0.01, 0.02, 0.05 mg/mL. For +S9: 0, 0.05, 0.1, 0.2 mg/mL. All tests in duplicates.

Test Results

Organ	*Effect*	*Rev.*	*OnSet*	*Sex*	*Affected in Exposed - Controls*
	MUT				

The test substance was positive for mutagenic effects in cultures with and without metabolic activation.

References

Primary Reference : **#URMMT***
Unpublished Report on Mutagenicity Test conducted by the Ministry of Health and Welfare (MHW), Japan, (1992)

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **MUTAGENICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	*Medium*	*Specification*	*Route*	*Lifestage*	*Sex*	*Number exposed*	*Number controls*
MOUSE							

Species/strain/system : Mouse, Crj:BDF1

Test Substance

Purity Grade : **>98%**

Test Method and Conditions

Test method description : OECD Test Guideline 474; micronucleus test. GLP: yes

Exposure

Exposure Type : **SHORT**

Exposure comments : Micronucleus test was performed with the following dose levels: males: 0, 150, 300, 600 mg/kg females: 0, 250, 500, 1000 mg/kg

Test Results

Organ	*Effect*	*Rev.*	*OnSet*	*Sex*	*Affected in Exposed - Controls*
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CELL

The lowest concentration producing toxicity was 1500 mg/kg.

MUT

Positive result for mutagenicity was obtained in 1000 mg/kg female group.

References

Primary Reference : **#MHMHR***

Unpublished Report on Micronucleus Test of (special chemical), HPV/SIDS test conducted by MHW

Secondary Reference : **!SIDSP***

OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **IRRITATION**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	*Medium*	*Specification*	*Route*	*Lifestage*	*Sex*	*Number exposed*	*Number controls*
RBT			**SKN**	**ADULT**	**M**		

Species/strain/system : New Zealand Albino male rabbits

Exposure

Exposure Type : **SHORT**
Exposure comments : Official method for testing cosmetics and toiletries.

Test Results

Organ	*Effect*	*Rev.*	*OnSet*	*Sex*	*Affected in Exposed - Controls*
SKIN	**IRRIT**			**M**	

The test substance was found "slightly irritant" under the test conditions.

References

Primary Reference : **FCTOD7**
Guillot, J. P. et al. Food and Chemical Toxicology, 20, 563, (1982)

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **IRRITATION**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	*Medium*	*Specification*	*Route*	*Lifestage*	*Sex*	*Number exposed*	*Number controls*
RBT			**SKN**	**ADULT**	**M**		

Species/strain/system : New Zealand Albino male rabbits

Test Method and Conditions

Test method description : Proposed method by Association Francaise de Normalisation for testing chemicals.

Exposure

Exposure Type : **SHORT**

Test Results

Organ	Effect	Rev.	OnSet	Sex	Affected in Exposed - Controls
SKIN	**IRRIT**			**M**	

The test substance was found "slightly irritant" under the test conditions.

References

Primary Reference : **FCTOD7**
Guillot, J. P. et al. Food and Chemical Toxicology, 20, 563, (1982)

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **IRRITATION**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	Medium	Specification	Route	Lifestage	Sex	Number exposed	Number controls
RBT			**SKN**	**ADULT**	**M**		

Species/strain/system : New Zealand Albino male rabbits

Test Method and Conditions

Test method description : OECD Test Guideline.

Test Results

Organ	Effect	Rev.	OnSet	Sex	Affected in Exposed - Controls
SKIN	**NEF**			**M**	

The test substance was found "non-irritant", under the test conditions.

References

Primary Reference : **FCTOD7**
Guillot, J. P. et al. Food and Chemical Toxicology, 20, 563, (1982)

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **IRRITATION**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	Medium	Specification	Route	Lifestage	Sex	Number exposed	Number controls
RBT			**OCU**	**ADULT**	**M**		

Species/strain/system : New Zealand Albino male rabbits

Test Method and Conditions

Test method description : Official method for testing cosmetics and toiletries.

Exposure

Dose / Concentration : **100 mg**

Test Results

Organ	Effect	Rev.	OnSet	Sex	Affected in Exposed - Controls
EYE	**IRRIT**				

The test substance was found "very irritant" at the dose of 100 mg.

References

Primary Reference : **FCTOD7**
Guillot, J. P. Food and Chemical Toxicology, 20, 573, (1982)

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **IRRITATION**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	Medium	Specification	Route	Lifestage	Sex	Number exposed	Number controls
UNS			**OCU**				

Species/strain/system : No information provided

Test Method and Conditions

Test method description : OECD Guideline and proposed method by Association Francaise de Normalisation for testing chemicals.

Test Results

Organ	*Effect*	*Rev.*	*OnSet*	*Sex*	*Affected in Exposed - Controls*
EYE	**IRRIT**				

The test substance was found "very irritant" at the dose of 100 mg.

References

Primary Reference : **FCTOD7**
Guillot, J. P. Food and Chemical Toxicology, 20, 573, (1982)

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **REPRODUCTION**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	*Medium*	*Specification*	*Route*	*Lifestage*	*Sex*	*Number exposed*	*Number controls*
RAT			**ORL**	**ADULT**	**M**	**12/GROUP**	**12**
					F	**12/GROUP**	**12**

Species/strain/system : Rat, Crj:CD(SD).

Test Substance

Purity Grade : **99%**
Vehicle - Solvent : Corn oil

Test Method and Conditions

Test method description : OECD Preliminary Reproduction Toxicity Screening Test. GLP: yes

Exposure

Exposure Type : **SHORT**
Dose / Concentration : **3-200 mg/kg**
Exposure comments : The doses of: 0, 3, 12, 50, 200 mg/kg/day were administered in oral gavage for 42 days to the male rats, and from 14 day before mating through day 3 of lactation to the female rats.

Test Results

Organ	*Effect*	*Rev.*	*OnSet*	*Sex*	*Affected in Exposed - Controls*
REPRO	**NEF**				

Copulation index and fertility index were not affected at all dose levels. Results applied to both female and male rats.

	DEATH		**F**

The dams of the 200 mg/kg/day group died on days 23 to 25 of pregnancy.

REPRO	**FUNCT**		**F**

Decrease in gestation index was observed under the test conditions in the groups of 50 and 200 mg/kg/day.

General Comments : 4-Ethoxyaniline produced the effects on general conditions (salivation) and food consumption of the males and the spleen (hypertrophy) of both sexes administered with more than 50 mg/kg, and the general conditions (salivation, cyanisis, delay of delivery period etc.) of the females and body weight of the males and food consumption of the females of the 200 mg/kg group. Reproductive toxicity observed in parental animals (fertility, gestation, reproductive organ toxicity, etc.). NOAEL for P generation = 50 mg/kg.

References

Primary Reference : **#MHRNB***
Unpublished Report on Preliminary Reproduction Toxicity Screening Test of (specific chemical)-HPV/SIDS test conducted by MHW, (1992)

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **TERATOGENICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	*Medium*	*Specification*	*Route*	*Lifestage*	*Sex*	*Number exposed*	*Number controls*
RAT			**ORL**	**ADULT**	**F**		

Species/strain/system : Rat, Crj:CD(SD)

Test Substance

Purity Grade : **>99%**
Vehicle - Solvent : Corn oil

Test Method and Conditions

Test method description : OECD Preliminary Reproduction Toxicity Screening Test. GLP: yes

Exposure

Exposure comments : Parental exposure doses of 0, 3, 12, 50, 200 mg/kg/day administered by oral gavage.

Test Results

Organ	*Effect*	*Rev.*	*OnSet*	*Sex*	*Affected in Exposed - Controls*
FETUS					

There was a decrease in survival index of offspring.

It was observed that the dams of the 200 mg/kg group died on day 23 to 25 of pregnancy. It is considered therefore that 4-ethoxyaniline produces some effects on prenatal period and neonatal development. NOAEL for F1 generation = 50 mg/kg.

References

Primary Reference : **#MHRNB***
Unpublished Report on Preliminary Reproduction Toxicity Screening Test of (specific chemical)-HPV/SIDS test conducted by MHW

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **AQUATIC ACUTE TOXICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**

Species/strain/system : Orange-red Killifish (Oryzias latipes)
Exposure Period : **48 h**

Test Results

Organism	*Medium*	*Spec.*	*Route*	*Lifestage*	*Sex*	*Effect*	*Effect Comments*
FISH	**AQ**	**FRESH**				**LC50**	LC50 for 48 hours = 234 mg/L. (Reported as ppm).

References

Primary Reference : **CMSHAF**
Yoshioka, V. et al. Chemosphere. Chemistry, Biology and Toxicology as related to Environmental Problems, 15(2), 195-203, (1986)

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **AQUATIC ACUTE TOXICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**

Species/strain/system : Orange-red Killifish (Oryzias latipes)
Exposure Period : **48 h**
Dose / Concentration : **100 mg/L**

Test Method and Conditions

Test method description : Model : JIS K0102. Static test. GLP: No

Test Results

Organism	*Medium*	*Spec.*	*Route*	*Lifestage*	*Sex*	*Effect*	*Effect Comments*
FISH	**AQ**	**FRESH**				**LC50**	LC50 for 48 hours = 100 mg/L (w/v). (Reported as ppm).

General Comments : Values are calculated.

References

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **AQUATIC TOXICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	*Medium*	*Specification*	*Route*	*Lifestage*	*Sex*	*Number exposed*	*Number controls*

ALGAE

Species/strain/system : Algae (Selenastrum capricornutum)

Test Substance

Purity Grade : **>99%**

Test Method and Conditions

Test method description : OECD Guideline. GLP: No

Exposure

Exposure Period : **72 h**

Test Results

Organ	*Effect*	*Rev.*	*OnSet*	*Sex*	*Affected in Exposed - Controls*
---	---	---	---	---	---
	EC50				

EC50 for 72 hours = 5.1 mg/L (w/v).

General Comments : Activity increases only gradually.

References

Primary Reference : **#EAATU***
Unpublished Report on Toxicity of (specific chemical) to Algae- HPV/SIDS test conducted by EA

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **AQUATIC TOXICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	*Medium*	*Specification*	*Route*	*Lifestage*	*Sex*	*Number exposed*	*Number controls*
CRUS	**AQ**	**FRESH**					

Species/strain/system : Water flea (Daphnia magna)

Test Substance

Purity Grade : **>99%**

Test Method and Conditions

Test method description : OECD Guideline. GLP: No. Calculation method: Probit method.

Exposure

Exposure Type : **ACUTE**
Exposure Period : **24 h**

Test Results

Organ	*Effect*	*Rev.*	*OnSet*	*Sex*	*Affected in Exposed - Controls*
---	---	---	---	---	---

EC0

EC0 for 24 hours = 10 mg/L (w/v). (Reported as ppm).

EC50

EC50 for 24 hours = 170 mg/L (w/v). (Reported as ppm).

EC100

EC100 for 24 hours = 1000 mg/L (w/v). (Reported as ppm).

References

Primary Reference : **#EADGP***
Unpublished Report on Toxicity of (specific chemical) to Daphnids-HPV/SIDS test conducted by EA

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **AQUATIC TOXICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	*Medium*	*Specification*	*Route*	*Lifestage*	*Sex*	*Number exposed*	*Number controls*
CRUS	**AQ**	**FRESH**					

Species/strain/system : Water flea (Daphnia magna)

Test Substance

Purity Grade : **>99%**

Test Method and Conditions

Test method description : OECD Guideline. Static test. GLP: No

Exposure

Exposure Type : **LONG**
Exposure Period : **21 d**

Test Results

Organ	*Effect*	*Rev.*	*OnSet*	*Sex*	*Affected in Exposed - Controls*
---	---	---	---	---	---

NOEL

No observed effect concentration (maximum) for 21 days = 0.19 mg/L (w/v). (Reported as ppm).

LOEL

(Lowest) first observed effect concentration (minimum) for 21 days = 0.6 mg/L (w/v). (Reported as ppm).

References

Primary Reference : **#EADGP***
Unpublished Report on Toxicity of (specific chemical) to Daphnids-HPV/SIDS test conducted by EA

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Study

End Point : **AQUATIC TOXICITY**
Chemical Name : **Benzenamine, 4-ethoxy-**
CAS Number : **156-43-4**
Study type : **LAB**

Test Subject

Organism	*Medium*	*Specification*	*Route*	*Lifestage*	*Sex*	*Number exposed*	*Number controls*
FISH	**AQ**	**FRESH**					

Species/strain/system : Orange-red Killifish (Oryzias latipes)

Test Substance

Vehicle - Solvent : DMSO: HCO = 4:1

Test Method and Conditions

Test method description : OECD Guideline. Semi-static test. GLP: No

Exposure

Exposure Type : **ACUTE**
Exposure Period : **24-96 h**
Exposure comments : Doses were also tested for 48 hours and 72 hours.

Test Results

Organ	*Effect*	*Rev.*	*OnSet*	*Sex*	*Affected in Exposed - Controls*
---	---	---	---	---	---

LC0

LC0 for 24, 48 and 72 hours = 180 mg/L (w/v), for 96 hours = 100 mg/L (w/v). (Reported as ppm (w/v)).

LC50

LC50 for 24 hours = 324 mg/L, for 48 hours = 300 mg/L, for 72 hours = 280 mg/L, for 96 hours = 240 mg/L.

LC100

LC100 for 24, 48, 72 and 96 hours = 583 mg/L (w/v). (Reported as ppm (w/v)).

References

Primary Reference : **#EAFGP***
Unpublished Report on Toxicity to Fish-HPV/SIDS test conducted by the EA

Secondary Reference : **!SIDSP***
OECD/SIDS. Screening Information Data Set (SIDS) of OECD High Production Volume Chemicals Programme, (1994)

Substance

[redacted]

Chemical Name : **P-PHENETIDINE**
Reported Name : **P-PHENETIDINE**
CAS Number : **156-43-4**

Area	*Type*	*Subject*	*Spec.*	*Description*	*Level / Summary Information :*
CAN	**REG**	**USE STORE LABEL**	**OCC**	**RQR**	INGREDIENT DISCLOSURE LIST CONCENTRATION 1% WEIGHT/WEIGHT. THE WORKPLACE HAZARDOUS MATERIALS INFORMATION SYSTEM (WHMIS) IS A NATIONAL SYSTEM TO PROVIDE INFORMATION ON HAZARDOUS MATERIALS USED IN THE WORKPLACE. WHMIS IS IMPLEMENTED BY THE HAZARDOUS PRODUCTS ACT AND THE CONTROLLED PRODUCTS REGULATIONS (ADMINISTERED BY THE DEPARTMENT OF CONSUMER AND CORPORATE AFFAIRS). THE REGULATIONS IMPOSE STANDARDS ON EMPLOYERS FOR THE USE, STORAGE AND HANDLING OF CONTROLLED PRODUCTS AND ADDRESS LABELLING AND IDENTIFICATION, EMPLOYEE INSTRUCTION AND TRAINING, AS WELL AS THE UPKEEP OF A MATERIALS SAFETY DATA SHEET (MSDS). THE PRESENCE IN A CONTROLLED PRODUCT OF AN INGREDIENT IN A CONCENTRATION EQUAL TO OR GREATER THAN SPECIFIED IN THE INGREDIENT DISCLOSURE LIST MUST BE DISCLOSED IN THE SAFETY DATA SHEET. ***Title :***

Reference : ***Effective Date :*** 31DEC1987

Last Amendment : **CAGAAK, 122, 2, 551, 1988** ***Entry / Update :*** APR1991
CANADA GAZETTE PART II

Substance

[redacted]

Chemical Name :
Reported Name : **p-phenetidine**
CAS Number : **156-43-4**

Area	*Type*	*Subject*	*Spec.*	*Description*	*Level / Summary Information :*
CSK	**REG**	**CLASS**	**-**	**CLASS**	THIS SUBSTANCE IS CLASSIFIED AS POISON. ***Title :*** GOVERNMENT PROVISION NO. 192 ON POISONS AND A NOTHER SUBSTANCES HARMFUL TO HUMAN HEALTH

Reference : **SZCSR*, 42, 1217, 1988** ***Effective Date :*** MAY1990
SBIRKA ZAKONU CESKOSLOVENSKE SOCIALISTICKE REPUBLIKY (COLLECTION OF THE LAW OF CZECHOSLOVAK SOCIALIST REPUBLIC)

Last Amendment : **SZCSR*, 33, 762, 1990** ***Entry / Update :*** DEC1991
SBIRKA ZAKONU CESKOSLOVENSKE SOCIALISTICKE REPUBLIKY (COLLECTION OF THE LAW OF CZECHOSLOVAK SOCIALIST REPUBLIC)

Substance

[redacted]

Chemical Name :
Reported Name : **p-phenetidine**
CAS Number : **156-43-4**

Area	*Type*	*Subject*	*Spec.*	*Description*	*Level / Summary Information :*
DEU	**REG**	**CLASS LABEL PACK**	**-**	**CLASS RQR RQR**	CLASSIFICATION AND LABELLING IN GERMANY IS GE NERALLY THE SAME AS FOR THE EEC (SEE OJEC** L 180, 1991). HOWEVER, SLIGHT MODIFICATIONS MAY BE INTRODUCED FOR SOME SUBSTANCES IN THE GER MAN LEGISLATION. ***Title :*** ORDINANCE ON HAZARDOUS SUBSTANCES. (GEFAHRSTO FFVERORDNUNG) ***Reference :*** **BGZBAD, I, 1931, 1991** ***Effective Date :*** 15JUN1991 **Bundesgesetzblatt. Federal Law Gazette** ***Last Amendment :*** ***Entry / Update :*** APR1992

Substance

Chemical Name :
Reported Name : **P-PHENETHIDINE**
CAS Number : **156-43-4**

Area	*Type*	*Subject*	*Spec.*	*Description*	*Level / Summary Information :*
RUS	**REG**	**AIR**	**OCC**	**MAC CLASS**	CLV: 0.2MG/M3 (VAPOUR) HAZARD CLASS: II ***Title :*** ***Reference :*** ***Effective Date :*** 01JAN1989 ***Last Amendment :*** **GOSTS*, 12.1.005, 1988** ***Entry / Update :*** MAY1990 **GOSUDARSTVENNYI STANDART SSSR (STATE STANDARD OF USSR)**

Substance

Chemical Name :
Reported Name : **p-phenetidine**
CAS Number : **156-43-4**

Area	*Type*	*Subject*	*Spec.*	*Description*	*Level / Summary Information :*
RUS	**REG**	**AQ**	**SURF**	**MAC CLASS**	0.02MG/L HAZARD CLASS: II ***Title :*** ***Reference :*** ***Effective Date :*** 1JAN1989 ***Last Amendment :*** **SPNPV*, 4630-88, 1988** ***Entry / Update :*** JUL1990 **SANITARNYE PRAVILA I NORMY OKHRANY POVERKHNOSTNYKH VOD OT ZAGRIAZNENIA (HEALTH REGULATION AND STANDARDS OF SURFACE WATER PROTECTION FROM CONTAMINATION)**

Substance

Chemical Name :
Reported Name : **p-phenetidine**
CAS Number : **156-43-4**

Area	*Type*	*Subject*	*Spec.*	*Description*	*Level / Summary Information :*
EEC	**REG**	**CLASS** **LABEL** **PACK**	**-**	**CLASS** **RQR** **RQR**	CLASS: T - TOXIC; TOXIC BY INHALATION, IN CON TACT WITH SKIN AND IF SWALLOWED (R 23/24/25). DANGER OF CUMULATIVE EFFECTS (R 33). LABEL: T - TOXIC; TOXIC BY INHALATION, IN CONTACT WI TH SKIN AND IF SWALLOWED (R 23/24/25); DANGER OF CUMULATIVE EFFECTS (R 33); WEAR SUITABLE PROTECTIVE CLOTHING AND GLOVES (S 36/37); AFT ER CONTACT WITH SKIN, WASH IMMEDIATELY WITH P LENTY OF... (TO BE SPECIFIED BY THE MANUFACTU RER) (S 28); IN CASE OF ACCIDENT OR IF YOU FE EL UNWELL, SEEK MEDICAL ADVICE IMMEDIATELY (S HOW THE LABEL WHERE POSSIBLE) (S 45). IT MUST BE STATED ON THE LABEL WHETHER IT IS A SPECI FIC ISOMER OR A MIXTURE OF ISOMERS. ***Title :*** COUNCIL DIRECTIVE 67/548/EEC OF 27 JUNE 1967 ON THE APROXIMATION OF THE LAWS, REGULATIONS AND ADMINISTRATIVE PROVISIONS RELATING TO THE CLASSIFICATION, PACKAGING AND LABELLING OF D ANGEROUS SUBSTANCES ***Reference :*** **OJEC**, 196, 1, 1967** ***Effective Date :*** 1JUL1992 **Official Journal of the European Communities** ***Last Amendment :*** **OJEC**, L 180, 79, 1991** ***Entry / Update :*** APR1992 **Official Journal of the European Communities**