

I U C L I D

D a t a S e t

Existing Chemical ID: 97-99-4
CAS No. 97-99-4
EINECS Name 2-Furanmethanol, tetrahydro-
EC No. 202-625-6
Molecular Formula C5H10O2

Producer Related Part

Company: National Institute of Health & Sciences
Creation date: 27-DEC-2004

Substance Related Part

Company: National Institute of Health & Sciences
Creation date: 27-DEC-2004

Memo: OECD HPV Chemicals programme, SIDS Dossier, approved at
SIAM 20 (19-21 April 2005)

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(DE), TA-Luft (DE), Material Safety Dataset, Risk
Assessment, Directive 67/548/EEC, SIDS

1. General Information

1.0.1 Applicant and Company Information

Type: lead organisation
Name: National Institute of Health & Sciences
Street: 1-18-1, Kamiyoga, Setagaya-ku
Town: 158-8501 Tokyo
Country: Japan
Phone: +81-3-3700-9878
Telex: 03-3700-1408

27-DEC-2004

Type: cooperating company
Name: National Institute of Environmental Studies, Environment
Agency
Street: 16-2, Onogawa
Town: 305-0053 Tsukuba-Ibaraki
Country: Japan
Phone: +81-29-850-2458
Telefax: +81-29-850-2920

27-DEC-2004

Type: cooperating company
Name: Chemicals Evaluation and Research Institute (CERI)
Street: 1-4-25 Koraku, Bunkyo-ku
Town: 112-0004 Tokyo
Country: Japan
Phone: +81-3-5804-6134
Telefax: +81-3-5804-6140

27-DEC-2004

1.0.2 Location of Production Site, Importer or Formulator

Type: manufacturer
Name of Plant: Koatsu Chemical Industries, Ltd.
Street: 1-12, Tsurumachi 5-chome, Taisyoku-ku
Town: 551-0023 Osaka
Country: Japan
Phone: +81-6-6552-0153
Telefax: +81-6-6552-0226

27-DEC-2004

1.0.3 Identity of Recipients

-

1.0.4 Details on Category/Template

-

1. General Information

1.1.0 Substance Identification

IUPAC Name: 2-Furanmethanol, tetrahydro-
 Smiles Code: O(C(CC1)CO)C1
 Mol. Formula: C5H10O2
 Mol. Weight: 102.13

Remark: Reference for Smiles Code: EPIWIN
 27-DEC-2004

1.1.1 General Substance Information

Purity type: measured for specific batch
 Substance type: organic
 Physical status: liquid
 Purity: = 99.3 - % w/w
 Colour: Colourless transparent liquid

27-DEC-2004 (10)

1.1.2 Spectra

-

1.2 Synonyms and Tradenames

Tetrahydro-2-furanmethanol

27-DEC-2004 (14)

2-Furanmethanol, tetrahydro-

Remark: IUPAC name
 27-DEC-2004 (2)

2-Hydroxymethyl oxolane

27-DEC-2004 (39)

Tetrahydro-2-furancarbinol

27-DEC-2004 (39)

Tetrahydro-2-furylmethanol

27-DEC-2004 (14)

Tetrahydrofurfuryl alcohol

27-DEC-2004 (14)

1. General Information

Tetrahydrofurfuryl alcohol

27-DEC-2004 (39)

THFA

27-DEC-2004 (14)

1.3 Impurities

Purity type: measured for specific batch

CAS-No: 7732-18-5

EC-No: 231-791-2

EINECS-Name: water

Mol. Formula: H₂O

Contents: = .1 - % w/w

Remark: Supplier: Wako Pure Chemical Ltd.

Lot No. SEF4748

Purity: 99.3 %

Impurity: water=0.1%

Unknown=0.6%

05-JAN-2005 (10)

1.4 Additives

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1.5 Total Quantity

Quantity: ca. 30 tonnes produced in 2003

Remark: A global production volume is unknown.

Annual production volume in Japan is ca. 30/tonnes (2003).

27-DEC-2004 (22)

1.6.1 Labelling

Labelling: as in Directive 67/548/EEC

Symbols: (Xi) irritating

R-Phrases: (36) Irritating to eyes

S-Phrases: (39) Wear eye/face protection

Remark: Labelling data were based on ICSC

27-DEC-2004 (39)

1.6.2 Classification

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1. General Information

1.6.3 Packaging

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1.7 Use Pattern

Type: industrial

Category: Basic industry: basic chemicals

01-JUL-2005

(22)

Type: industrial

Category: Chemical industry: used in synthesis

27-DEC-2004

(22)

Type: industrial

Category: Paints, lacquers and varnishes industry

01-JUL-2005

(22)

Type: use

Category: Intermediates

01-JUL-2005

(22)

Type: type

Category: Use resulting in inclusion into or onto matrix

01-JUL-2005

(22)

Type: type

Category: Wide dispersive use

01-JUL-2005

Type: use

Category: Solvents

01-JUL-2005

1.7.1 Detailed Use Pattern

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1.7.2 Methods of Manufacture

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1.8 Regulatory Measures

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1. General Information

1.8.1 Occupational Exposure Limit Values

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1.8.2 Acceptable Residues Levels

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1.8.3 Water Pollution

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1.8.4 Major Accident Hazards

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1.8.5 Air Pollution

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1.8.6 Listings e.g. Chemical Inventories

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1.9.1 Degradation/Transformation Products

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1.9.2 Components

-

1.10 Source of Exposure

-

1.11 Additional Remarks

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1.12 Last Literature Search

Type of Search: Internal and External

Chapters covered: 1

Date of Search: 27-DEC-2004

27-DEC-2004

Type of Search: Internal and External

Chapters covered: 2

Date of Search: 27-DEC-2004

27-DEC-2004

date: 11-JAN-2006

1. General Information

Substance ID: 97-99-4

Type of Search: Internal and External

Chapters covered: 3

Date of Search: 27-DEC-2004

27-DEC-2004

1.13 Reviews

-

2. Physico-chemical Data

2.1 Melting Point

Value: < -120 degree C
 Decomposition: no at degree C

Method: OECD Guide-line 102 "Melting Point/Melting Range"
 Year: 2004
 GLP: yes

Remark: A study was conducted according to OECD Test Guideline 102
 "Melting point/Melting range: Differential Scanning
 Carolimetry (DSC)".
 No clear melting point was observed in a range of 100 to
 -120 degree C.

Test substance: Supplier: Wako Pure Chemical Ltd.
 Lot No. SEF4748
 Purity: 99.3 %
 Impurity: water=0.1%
 Unknown=0.6%

Reliability: (2) valid with restrictions
 Guideline study conducted under GLP condition.
 No clear melting point/range was reported.

06-JAN-2005

(8)

Value: = -20.9 degree C

Method: other: Calculated by MPBPWIN v.1.41, 2000
 Year: 2000

Method: Mean or Weighted MP.
 Reliability: (2) valid with restrictions
 Accepted calculation method.

05-JAN-2005

(11)

Value: < -80 degree C

Method: other: Not specified
 Year: 2003
 Test substance: other TS: Not specified.

Source: CRC Handbook of Chemistry and Physics.

Reliability: (2) valid with restrictions
 Data from peer reviewed data source.

Flag: Critical study for SIDS endpoint

05-JAN-2005

(16)

2.2 Boiling Point

Value: = 177.7 degree C at 1013 hPa

Method: OECD Guide-line 103 "Boiling Point/boiling Range"
 Year: 2004
 GLP: yes

Method: A study was conducted according to Siwoloboff method.
 Result: 177.6, 177.7 degree C. (Av. 177.7 degree C)
 Test substance: Supplier: Wako Pure Chemical Ltd.
 Lot No. SEF4748
 Purity: 99.3 %
 Impurity: water=0.1%
 Unknown=0.6%

Reliability: (1) valid without restriction
 Guideline study conducted under GLP condition.

Flag: Critical study for SIDS endpoint
 06-JAN-2005 (6)

Value: = 172.4 degree C

Method: other: Calculated by MPBPWIN v.1.41 (2000)
 Year: 2000

Method: Adapted Stein & Brown method.
 Reliability: (2) valid with restrictions
 Accepted calculation method.
 06-JAN-2005 (11)

Value: = 178 degree C at 1013

Method: other: not specified
 Year: 2003
 Test substance: other TS: not specified

Source: CRC Handbook of Chemistry and Physics.
 Reliability: (2) valid with restrictions
 Data from peer reviewed data source.
 05-JAN-2005 (16)

2. Physico-chemical Data

2.3 Density

Type: relative density
 Value: = 1.0544 at 20 degree C

Method: other: not specified
 Year: 2003
 Test substance: other TS: not specified

Source: CRC Handbook of Chemistry and Physics.
 Reliability: (2) valid with restrictions
 Data from peer reviewed data source.
 Flag: Critical study for SIDS endpoint
 05-JAN-2005 (16)

Type: relative density
 Value: = 1.0558 at 20 degree C

Year: 2004

Reliability: (4) not assignable
 Manufacture data without proof.
 Flag: Material Safety Dataset
 05-JAN-2005 (10)

2.3.1 Granulometry

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2.4 Vapour Pressure

Value: = 1.86 hPa at 25 degree C

Method: OECD Guide-line 104 "Vapour Pressure Curve"
 Year: 2004
 GLP: yes

Method: Measured according to static method.
 Result: Measurements were carried out at 40, 50 and 60 degree C
 (n=3).

	C	VP (hPa)
Temp. 40		3.99, 3.99, 3.99
	50	5.99, 5.99, 5.99
	60	9.98, 9.98, 9.31

A vapour pressure at 25 degree C was obtained by extrapolation.

Test substance: Supplier: Wako Pure Chemical Ltd.
 Lot No. SEF4748
 Purity: 99.3 %
 Impurity: water=0.1%
 Unknown=0.6%

Reliability: (1) valid without restriction
 Guideline study conducted under GLP condition.
 Flag: Critical study for SIDS endpoint

06-JAN-2005 (12)

Value: = .3625 hPa at 25 degree C

Method: other (calculated): MPBPWIN v.1.41, 2000

Reliability: (2) valid with restrictions
Accepted calculation method.

05-JAN-2005 (11)

Value: = 1.066 hPa at 25 degree C

Year: 1989

Source: Physical and Thermodynamic Properties of Pure Chemicals Data
Compilation.

Reliability: (2) valid with restrictions
Data from reliable handbook or collection of data.

05-JAN-2005 (17)

2.5 Partition Coefficient

Partition Coeff.: octanol-water
log Pow: = -.11 at 20 degree C

Method: OECD Guide-line 107 "Partition Coefficient (n-octanol/water),
Flask-shaking Method"

Year: 2004

GLP: yes

Test condition: Condition:

Octanol (ml)	Water (ml)	Test substance (mg)
5	30	5.0
10	25	5.0
20	15	5.0

Analytical method:
Gas chromatography with external standard.

Result: (log value)

Condition-1	Condition-2	Condition-3
-0.11	-0.11	-0.11
-0.11	-0.11	-0.11

Overall average value = -0.11

Test substance: Supplier: Wako Pure Chemical Ltd.

Lot No. SEF4748

Purity: 99.3 %

Impurity: water=0.1%

Unknown=0.6%

Reliability: (1) valid without restriction

2. Physico-chemical Data

Guideline study conducted under GLP condition.
 Flag: Critical study for SIDS endpoint
 06-JAN-2005 (9)

Partition Coeff.: octanol-water
 log Pow: = -.11

Method: other (calculated): KOWWIN v.1.66
 Year: 2004

Reliability: (2) valid with restrictions
 Accepted calculation method.
 05-JAN-2005 (11)

2.6.1 Solubility in different media

Solubility in: Water
 Value: > 250 g/l at 20 degree C
 pH value: = 4.6 - 4.7
 Conc.: 250 g/l at 20 degree C

Method: OECD Guide-line 105
 Year: 2004
 GLP: yes

Method: 1.25 g of test substance was added in 5 ml of distilled
 water (n=3).
 Test solutions were shaken at 20 degree C for one hours and
 left standing for another 2 hours.
 Visually confirmed the complete dissolution and checked by
 GC analysis

Test substance: Supplier: Wako Pure Chemical Ltd.
 Lot No. SEF4748
 Purity: 99.3 %
 Impurity: water=0.1%
 Unknown=0.6%

Reliability: (1) valid without restriction
 Guideline study conducted under GLP condition.
 Flag: Critical study for SIDS endpoint
 06-JAN-2005 (13)

Solubility in: Water
 Value: = 463.4 g/l at 25 degree C

Method: other: calculated by WSKOW v1.40. (2000)
 Year: 2004

Reliability: (2) valid with restrictions
 Accepted calculation method.
 06-JAN-2005 (11)

Solubility in: other

Remark: Miscible with water, alcohol, ether, acetone, chloroform and benzene

Source: The Merck Index.

Reliability: (2) valid with restrictions
Data from peer reviewed data source.

06-JAN-2005 (3)

2.6.2 Surface Tension

Test type: other: not specified
Value: = .037 mN/m at 25 degree C

Method: other: not specified

Source: The Merck Index

Reliability: (2) valid with restrictions
Data from peer reviewed data source.

Flag: Critical study for SIDS endpoint

06-JAN-2005 (3)

2.7 Flash Point

Value: = 75 degree C
Type: open cup

Year: 1997

Source: Fire Protection Guide to Hazardous Materials.

Reliability: (2) valid with restrictions
Data from peer reviewed data source.

Flag: Critical study for SIDS endpoint

06-JAN-2005 (19)

2.8 Auto Flammability

Value:

Remark: Autoignition Temperature = 282 degree C.

Source: Fire Protection Guide to Hazardous Materials. 12 ed

Reliability: (2) valid with restrictions
Data from peer reviewed data source.

Flag: Critical study for SIDS endpoint

06-JAN-2005 (19)

2.9 Flammability

Result: flammable

Year: 1997

Remark: Flammable Limits:
Lower flammable limit = 1.5% by volume, Upper flammable
limit = 9.7% by volume.

Reliability: (2) valid with restrictions
Data from peer reviewed data source.

Flag: Critical study for SIDS endpoint

06-JAN-2005

(19)

2.10 Explosive Properties

Result: explosive under influence of a flame

Year: 1996

Remark: Lower explosive limit: 1.5% Upper explosive limit: 9.7% @
22.2 to 50 degree C.

Source: Lewis, R.J. Sax's Dangerous Properties of Industrial
Materials.

Reliability: (2) valid with restrictions
Data from peer reviewed data source.

Flag: Critical study for SIDS endpoint

06-JAN-2005

(24)

2.11 Oxidizing Properties

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2.12 Dissociation Constant

-

2.13 Viscosity

Value: = 6.24 mPa s (dynamic) at 20 degree C

Year: 1996

Source: The Merck Index

Reliability: (2) valid with restrictions
Data from peer reviewed data source.

Flag: Critical study for SIDS endpoint

06-JAN-2005

(3)

2.14 Additional Remarks

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3.1.1 Photodegradation

Type: air
 INDIRECT PHOTOLYSIS
 Sensitizer: OH
 Conc. of sens.: 1500000
 Rate constant: = .00000000002358 cm³/(molecule * sec)
 Degradation: = 50 % after .5 day(s)

Method: other (calculated): AOPWIN v1.90
 Year: 2004

Remark: Calculated by SRC-AOPWIN v1.90.
 Based on 12hrs/day irradiation.

Reliability: (2) valid with restrictions
 Valid calculation method.

Flag: Critical study for SIDS endpoint
 06-JAN-2005

(11)

3.1.2 Stability in Water

Type: abiotic
 t1/2 pH4: > 1 year at 25 degree C
 t1/2 pH7: > 1 year at 25 degree C
 t1/2 pH9: > 1 year at 25 degree C
 Deg. products: no

Method: OECD Guide-line 111 "Hydrolysis as a Function of pH"
 Year: 2004
 GLP: yes

Method: 20 mg/l of test substance solutions at pHs 4, 7 and 9 were
 incubated at 50 degree C for 5 days (n=2).
 Concentrations after incubation were determined by gas
 chromatography.
 More than 90 % of the initial concentration was maintained
 in all vessels.

Result: The test substance was stable in water and its half-life at
 25 degree C was calculated more than 1 year at pHs 4, 7 and
 9.

Reliability: (1) valid without restriction
 Guideline study conducted under GLP condition.

Flag: Critical study for SIDS endpoint
 06-JAN-2005

(7)

Type: abiotic

Method: other
Year: 1990

Remark: 2-Furanmethanol, tetrahydro- is not expected to undergo hydrolysis in the environment due to the lack of hydrolyzable functional groups.

Source: Handbook of Chemical Property Estimation Methods.

Reliability: (2) valid with restrictions
Data from peer reviewed data source.

04-JUL-2005

(25)

3.1.3 Stability in Soil

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3.2.1 Monitoring Data (Environment)

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3.2.2 Field Studies

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3.3.1 Transport between Environmental Compartments

Type: volatility
Media: water - air
Method: other: calculated by HENRYWIN v3.10 (Bond Method)
Year: 2000

Remark: The Henry's Law Constant was calculated using a water solubility of 250 g/l, a vapour pressure of 1.395mmHg, a molecular weight of 102.13 and a temperature of 25 degree C.
Result: The calculated Henry's Law constant was 4.09x10⁻⁹ atm-m³/mole.

Reliability: (2) valid with restrictions
Accepted calculation method.

Flag: Critical study for SIDS endpoint

06-JAN-2005

(11)

3.3.2 Distribution

Media: air - biota - sediment(s) - soil - water
 Method: other (calculation): Level III Fugacity Model
 Year: 2004

Remark: The following input parameters were used for the calculation.

Molecular weight: 102.13
 Melting point (degree C): -80 (measured)
 Vapour pressure (mmHG): 1.395 (measured)
 Water solubility (g/l): 250 (measured)
 Log Kow: -0.11 (calculated)
 Temperature (degree C): 25

Result:

	Mass amount (%)	Half-life (h)	Emission (kg/h)
Air	1.67	10.9	1000
Water	54.3	360	1000
Soil	44	360	1000
Sediment	0.091	1440	0

Reliability: (2) valid with restrictions

Accepted calculation method.

Flag: Critical study for SIDS endpoint

12-AUG-2005

(11)

Media: water - soil

Method: other (calculation): PCKOCWIN v1.66

Year: 2004

Result: Calculated Koc value is 1 (log Koc = 0.0)

Reliability: (2) valid with restrictions

Accepted calculation method.

Flag: Critical study for SIDS endpoint

06-JAN-2005

(11)

3.4 Mode of Degradation in Actual Use

-

3.5 Biodegradation

Type: aerobic
 Inoculum: activated sludge, non-adapted
 Concentration: 100 mg/l related to Test substance
 Contact time: 28 day(s)
 Degradation: = 90 - 94 % after 28 day(s)
 Result: readily biodegradable
 Kinetic: 7 day(s) = 15 - 67 %
 14 day(s) = 72 - 92 %
 21 day(s) = 87 - 92 %
 28 day(s) = 90 - 94 %

Control Subst.: Aniline
 Kinetic: 7 day(s) = 70 %
 14 day(s) = 75 %

Deg. product: no

Method: OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
 Year: 2004
 GLP: yes

Result: Following results were reported.

Biodegradation rates (28 days)

by BOD	92%	94%	90%	(Av. 92%)
by TOC	97%	98%	98%	(Av. 98%)
by GC	100%	100%	100%	(Av. 100%)

Three measurement methods (BOD, TOC and GC) suggested complete degradation.
 10-day window was also met.
 Oxygen uptake in the inoculum blank was 2.9 mg-O₂/L in 28 days.

Test condition: 30 mg of the test substance (n=3) or aniline (n=1) and 9 mg of activated sludge (as MLSS) were added into 300 ml of test medium.
 The test and control vessels were incubated for 28 days at 25 degree C.
 Biodegradabilities of the test and the control substance were continuously measured by BOD meter.
 After 28 days cultivation, residual amount of the test substance was determined by DOC and GC analysis.

Test substance: Supplier: Wako Pure Chemical Ltd.
 Lot No. SEF4748
 Purity: 99.3 %
 Impurity: water=0.1%
 Unknown=0.6%

Reliability: (1) valid without restriction
 Guideline study under GLP condition.

Flag: Critical study for SIDS endpoint
 12-AUG-2005

(5)

3. Environmental Fate and Pathways

3.6 BOD5, COD or BOD5/COD Ratio

-

3.7 Bioaccumulation

BCF: = 3.16

Method: other: calculated by BCFWIN v2.14

Year: 2004

Remark: Calculation was conducted based on a log Pow value of -0.11.

Reliability: (2) valid with restrictions

Accepted calculation method.

Flag: Critical study for SIDS endpoint

06-JAN-2005

(11)

3.8 Additional Remarks

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4. Ecotoxicity

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: semistatic
 Species: *Oryzias latipes* (Fish, fresh water)
 Exposure period: 96 hour(s)
 Unit: mg/l Analytical monitoring: yes
 LC0: > 101 - measured/nominal
 LC50: > 101 - measured/nominal
 Limit Test: yes

Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
 Year: 2003
 GLP: yes
 Test substance: other TS: E and E solutions Inc., Lot. No.;2002-4, Purity = 99.480%

Method: -Test Organisms:
 a) Supplier: Test organisms were obtained from private reproduction in Japan.
 b) Size (length and weight): 2.29cm (2.19 - 2.40cm) in length; 0.197 g (0.161 - 0.229 g) in weight.
 c) Age: About 1 year old.
 d) Any pretreatment: Test organisms were acclimated for 18 days before testing. During acclimation, test fishes were fed with TETRAMINE. The mortality of the test organisms for 7 days before testing was below 5%. LC50(96 hr) for a reference substance (copper sulfate pentahydrate) was 1.2 mg/L.

-Test substance: tetrahydrofurfurylalkohol
 a) Empirical Formula: C₅H₁₀O₂
 b) Molecular Weight: 102.13
 c) Purity: = 99.480 %
 d) Boiling Point: 178 C
 e) Water Solubility: High

-Test Conditions:
 a) Dilution Water Source: Tap water in Yokohama, Japan treated activate carbone, dechlorinated and fully aerated.
 b) Dilution Water Chemistry: pH: 7.6 (21 C)
 Total hardness (as CaCO₃): 73 mg/L
 c) Exposure Vessel Type: 5 L glass beaker
 d) Nominal Concentrations: control and 100 mg/L (limit test)
 e) Vehicle/Solvent and Concentrations: Not used.
 f) Stock Solutions Preparations and Stability: Test substance was diluted with dilution water. Test substance was stored in desiccator (room temperature, dark place, nitrogen inclusion). The stability of the chemical was confirmed by IR absorption spectrum. Under the stock condition, IR spectrum of the test substance at the end of

test was same at the start.

- g) Number of Replicate: 1
- h) Fish per Replicates: 10
- i) Renewal Rate of Test Water: 24 - hour intervals
- j) Water Temperature: 24+/-1C
- k) Light Condition: 16:8 hours, light-darkness cycle
- l) Feeding: None
- m) Aeration : None

-Analytical Procedure: The test concentrations were measured at the start, 48th and 96th hours using GC.

-Statistical Method:

- a) Data Analysis:None
- b) Method of Calculating Mean Measured Concentrations (i.e. arithmetic mean, geometric mean, etc.):Geometric mean

Result:

- Measured Concentrations: The test concentrations were measured at the start and before water replacemnt (24-hour) for the test using GC.

Nominal Conc.	Measured Conc. (mg/L)			Percent of Nominal (%)	
	0 Hour	24 Hour	Geo mean	0 Hour	24 Hour
Control	<0.3	<0.3	---	---	---
100	102	99.8	101	102	100

- Water chemistry (pH, DO and temperature in test): Water chemistry were measured for each concentration everyday.

- pH: 7.4 - 7.8
- DO: 6.1 - 8.5 mg/L
- Water Temperature: 23.6 - 24.1 C

-Effect Data(mortality):

- LC50 (96hr) > 101 mg/L (mc)
- LC0 (96hr) > 101 mg/L (mc)
- The LC50 value and its 95% confidence limits could not be determined because the test was conducted as a limit test.

- Cumulative Mortality: None of test organisms were killed during exposure period at both control and 100mg/L.

Measured Conc. Cumulative Number of Dead (Percent Mortality)

mg/L	24 Hour	48 Hour	72 Hour	96Hour
Control	0 (0)	0 (0)	0 (0)	0 (0)
101	0 (0)	0 (0)	0 (0)	0 (0)

-Other Effect: Symptoms of toxicity was not observed during test period.

- Calculation of toxicity values: The calculation of toxicity values was the measured concentration.

Source: National Institute for Environment Studies Ibaraki
Reliability: (1) valid without restriction
12-AUG-2005

(28)

4.2 Acute Toxicity to Aquatic Invertebrates

Type: semistatic
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: yes
NOEC: > 91.7 - measured/nominal
EC50: > 91.7 - measured/nominal
Limit Test: yes

Method: OECD Guide-line 202
Year: 2003
GLP: yes
Test substance: other TS:E and E solutions Inc., Lot. No.;2002-4, Purity = 99.480%

Method: -Test Organisms:
a) Age: < 24 hours old
b) Supplier/Source: Test organisms were obtained from the National Institute of Environmental Studies (Japan).
c) Any pretreatment: Parental daphnids were acclimated for 3 weeks on test condition before testing. During acclimatization, test daphnids were fed with Chlorella vulgaris, 0.2 mg carbon/day/individual. Juveniles in batches of high mortality and contain resting eggs and males were not used as test individuals. EC50 (48hr, immobility) for reference substance (potassium dichromate) was 0.75 mg/L.

-Test substance: tetrahydrofurfurylalkohol
a) Empirical Formula: C₅H₁₀O₂
b) Molecular Weight: 102.13
c) Purity: = 99.480 %
d) Boiling Point: 178 C
e) Water Solubility: High

-Test Conditions:
a) Dilution Water Source: Elendt M4
b) Dilution Water Chemistry:
c) Exposure Vessel Type: 100 mL test solution in a 100 mL glass beaker covered with teflon sheet on surface and cap.
d) Nominal Concentrations: control and 100 mg/L

- e) Vehicle/Solvent and Concentrations: Not used.
- f) Stock Solutions Preparations and Stability: Test substance was diluted with Elendt M4. Test substance was stored in desiccator (room temperature, dark place, nitrogen inclusion). The stability of the chemical was confirmed by IR absorption spectrum. Under the stock condition, IR spectrum of the test substance at the end of test was same at the start.
- g) Number of Replicates: 4
- h) Individuals per Replicates: 5
- i) Water Temperature: 20+/-1C
- j) Light Condition: 16:8 hours, light-darkness cycle
- k) Feeding: None
- l) Aeration : None

- Analytical Procedure: Test concentrations were measured at the start and the end of test using GC.

- Statistical Method:

- a) Data Analysis: None
- b) Method of Calculating Mean Measured Concentrations: Geometric mean.

Result:

- Measured Concentrations: The test concentrations were measured at the start and before water replacement (24th hour).

mg/L	Measured Conc., mg/L		Geomean	Percent of Nominal, %	
	0 Hour New	24 Hour Old		0 Hour New	24 Hour Old
Control	<0.3	<0.3	---	---	---
100	91.6	91.8	91.7	92	92

new: freshly prepared test solution.
 old: test solution after 48 hours exposure

- Water chemistry (pH, DO, temperature and total hardness in test): Water chemistry were measured for control and 100 mg/L at the start and before water replacement during test period.

- pH: 8.2 - 8.3
- DO: 8.5 - 8.8 mg/L
- Water Temperature: 19.6 - 20.0 C
- Total hardness (as CaCO3): 260 mg/L

-Effect Data:

- EC50 (48hr) > 91.7 mg/L (mc)
- NOEC (48hr) > 91.7 mg/L (mc)

-Mortality or Immobility: None of test organisms were

immobilized the behavior both control and 100mg/L.

 Cumulative Number of Immobilized Daphnia
 Measured (Percent Immobility)
 Conc.

mg/L	24 Hour	48 Hour
Control	0 (0)	0 (0)
91.7	0 (0)	0 (0)

- Calculation of toxic values: Measured concentration.

Source: National Institute for Environment Studies Ibaraki
 Reliability: (1) valid without restriction
 12-AUG-2005

(28)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: other algae: Pseudokirchneriella subcapitata
 Endpoint: growth rate
 Exposure period: 72 hour(s)
 Unit: mg/l Analytical monitoring: yes
 NOEC: > 98.9 - measured/nominal
 EC10: - measured/nominal
 EC50: > 98.9 -
 Limit Test: yes

Method: OECD Guide-line 201 "Algae, Growth Inhibition Test"
 Year: 2003
 GLP: yes
 Test substance: other TS:E and E solutions Inc., Lot. No.;2002-4, Purity = 99.480%

Method: -Test Organisms:
 a) Supplier/Source: Obtained from American Type Culture Collection.
 b) Method of Cultivation: Sterile
 c) Strain Number:ATCC22662
 d) Any pretreatment: Acclimated for 5 days before testing.

-Test substance: tetrahydrofurfurylalkohol
 a) Empirical Formula:C5H10O2
 b) Molecular Weight: 102.13
 c) Purity: = 99.480 %
 d) Boiling Point: 178 C
 e) Water Solubility: High

- Test Conditions:
 a) Medium: OECD medium

- b) Exposure Vessel Type: 100 mL Medium in a 300mL glass Erlenmeyer flask with breathable silicon cap.
- c) Nominal Concentrations: control and 100 mg/L
- d) Vehicle/Solvent and Concentrations: Not used
- e) Stock Solution Preparations and Stability: Test substance was diluted with OECD medium. Test substance was stored in desiccator (room temperature, dark place, nitrogen inclusion). The stability of the chemical was confirmed by IR absorption spectrum. Under the stock condition, IR spectrum of the test substance at the end of test was same at the start.
- f) Number of Replicates: 3
- g) Initial Cell Number: 10,000 cells/mL
- h) Water Temperature: 23+/-2C
- i) Light Condition: 4000 lux, continuously
- j) Shaking: 100 rpm

- Analytical Procedure: Test concentrations were measured at the start and the end of test using by GC after removing algal cells by a centrifuge.

- Statistical Method:

- a) Data Analysis: Student's t-test (a=0.05, both side) for NOEC, after homoscedastic test (F-test).
- b) Method of Calculating Mean Measured Concentrations (i.e. arithmetic mean, geometric mean, etc.): The measured concentration at start of the test was used for calculation.

Result:

- Measured Concentrations : Test concentrations were measured at the start and the end of test using by GC. All of them, the deviation from the nominal were less than +/- 10%.

Nominal Conc.	Measured Conc. mg/L		Percent of Nominal conc. %	
	0 Hour	72 Hour	0 Hour	72 Hour
Control	<0.2	<0.2	---	---
100	98.9	91.0	99	91

- Water chemistry (pH and temperature in test): pH was measured for control and 100mg/L at the start and the end of test. At the start and the end of test, the pH was 7.8 - 7.9 and 9.8- 10.2 respectively. Temperature in algal culture cabinet was measured at least once per day and maintained 23.0 C during test period.
 pH: 7.8 - 10.2
 temperature: 23 +/- 2 C

-Effect Data: Rate Method

4. Ecotoxicity

EC50 (0 - 72 hr) :> 98.9 mg/L

NOEC (0 - 72 hr) : > 98.9 mg/L

- Growth Inhibition (%) of *Pseudokirchneriella subcapitata*

Growth rate, Inhibition and Cell density

Measured

Conc. mg/L	Rate (Average) u(0-72hr)	Inhibition(%) Im(0-72hr)	Cell density(72hr)
Control	1.87	---	2752333
98.9	1.87	0.33	2702333

- Growth Curves: Exponential growth phase during 72 hours.

- Calculation of toxic value: Measured concentration at start of the test.

Source:

National Institute for Environment Studies Ibaraki

Reliability:

(1) valid without restriction

12-AUG-2005

(28)

4.4 Toxicity to Microorganisms e.g. Bacteria

-

4. Ecotoxicity

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

-

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
 Endpoint: reproduction rate
 Exposure period: 21 day(s)
 Unit: mg/l Analytical monitoring: yes
 NOEC: > 95.1 - measured/nominal
 LOEC: > 95.1 - measured/nominal
 EC50: > 95.1 - measured/nominal

Method: OECD Guide-line 211
 Year: 2003
 GLP: yes
 Test substance: other TS: E and E solutions Inc., Lot. No.;2002-4, Purity = 99.480%

Method: -Test Organisms:
 a) Age: < 24 hours old
 b) Supplier/Source: Test organisms were obtained from the National Institute of Environmental Studies (Japan).
 c) Any pretreatment: Parental daphnids were acclimated for 4 weeks on test condition before testing. During acclimatization, test daphnids were fed with Chlorella vulgaris, 0.2 mg carbon/day/individual. Mothers of test individuals were selected from batches which were not observed death individuals and any resting-eggs and male daphnia. EC50 (48hr, immobility) for reference substance (potassium dichromate) was 0.75 mg/L.

-Test substance: tetrahydrofurfurylalkohol
 a) Empirical Formula: C₅H₁₀O₂
 b) Molecular Weight: 102.13
 c) Purity: = 99.480 %
 d) Boiling Point: 178 C
 e) Water Solubility: High

-Test Conditions:
 a) Dilution Water Source: Elendt M4
 b) Dilution Water Chemistry:
 c) Exposure Vessel Type: 80 mL test solution in a 100 mL glass beaker covered with teflon sheet on surface and cap.
 d) Nominal Concentrations: control and 100 mg/L
 e) Vehicle/Solvent and Concentrations: Not used.
 f) Stock Solutions Preparations and Stability: Test substance was diluted with Elendt M4. Test substance was stored in desiccator (room temperature, dark place, nitrogen inclusion). The stability of the chemical was confirmed by

IR absorption spectrum. Under the stock condition, IR spectrum of the test substance at the end of test was same at the start.

- g) Number of Replicates: 10
- h) Individuals per Replicates: 1
- i) Water Temperature: 20+/-1C
- j) Light Condition: 16:8 hours, light-darkness cycle
- k) Feeding: 0.15 mg carbon/day/individual (Chlorella vulgaris: Green Algae)
- l) Aeration : None

- Analytical Procedure: The test concentrations were measured 3 times during test period for both renewal and old test solution using GC.

- Statistical Method:

a) Data Analysis:

LC50 and EC50: LC50 , EC50 and their 95%c.l. cannot be calculated.

NOEC and LOEC: The cumulative number of juveniles produced per adult in control and 100mg/L after 21days was tested by Student's t-test (show homoscedasticity on F-test) or Welch's t-test (show nonhomoscedasticity on F-test) (Statlight, Yukms Corp., Tokyo).

b) Method of Calculating Mean Measured Concentrations (i.e. arithmetic mean, geometric mean, etc.): Time-weighted Mean

Result:

- Effect: reproduction- Measured Concentrations: The test concentrations were measured for both renewal and old test solution at the start of the test and 1st, 7th, 8th, 14th and 15th day.

Nominal Conc.	Measured Concentration, mg/L							
mg/L	Date	0	1	7	8	14	15	TWM*
		New	Old	New	Old	New	Old	(mg/L)
Control		<0.3	<0.3	<0.3	<0.3	<0.3	<0.3	---
100		96.1	95.4	96.1	95.2	94.6	93.5	95.1

new: freshly prepared test solution.

old: test solutions 24 hours before water renewal.

*: Time-weighted mean measured concentration during 21days.

Nominal Conc.	Percent of Nominal Conc. (%)							
mg/L	Date	0	1	7	8	14	15	TWM*
		New	Old	New	Old	New	Old	(mg/L)
Control		---	---	---	---	---	---	---

100 96 95 96 95 95 94 95

new: freshly prepared test solution.
old: test solutions 24 hours before water renewal.
*: Time-weighted mean measured concentration during 21days.

- Water chemistry (pH, DO, temperature and total hardness in test): Water chemistry and temperature were measured for control and 100mg/L at 4 times (before and after water renewal).
pH: 7.6 - 8.3
DO: 7.3 - 8.8 mg/L
Water Temperature: 19.6 - 20.4 C
Total hardness (as CaCO3): 245 - 270 mg/L

-Effect Data(Reproduction):
LC50 (21days) > 95.1 mg/L (parental mortality) (mc)
EC50 (21days) > 95.1 mg/L (mc)
NOEC (21days) > 95.1 mg/L
LOEC (21days) > 95.1 mg/L
mc: based on Time-weighted mean of measured concentrations

- Cumulative Number of Died Parental Daphnia: Mortality rate of parental daphnia both control and 100mg/L were 0%.

-Time (days) to First Brood Production: All parental daphnia first brood at 8 days.

-Cumulative numbers of juveniles produced per adult

Measured Conc. mg/L	Mean Cumulative Numbers of Juveniles Produced per Adult for 21 days								
	0	7	8	9	10	11	12	13	14
Control	0	0	9.9	9.9	9.9	33.7	33.7	33.7	41.0
95.1	0	0	7.7	7.7	7.7	27.5	29.1	29.2	43.7

Measured Conc. mg/L	Mean Cumulative Numbers of Juveniles Produced per Adult for 21 days						
	15	16	17	18	19	20	21
Control	58.6	58.6	58.6	88.6	88.6	88.6	115.3
95.1	55.7	55.7	58.5	85.7	85.7	85.7	113.9

-Cumulative numbers of juveniles produced per adult alive for 21 days

Nominal Concentration, mg/L
(Measured Concentration, mg/L)

Vessel No.	Control	100 (95.1)
1	114	117
2	118	119
3	112	116
4	114	113
5	104	116
6	117	110
7	122	108
8	122	121
9	118	117
10	112	102
Mean	115.3	113.9
S.D.	5.4	5.7
Inhibition ratio (%)		1.2
Significant difference		---

--- : Indicate a no-significant difference.

- Calculation of toxicity values: The calculation of toxicity values was the Time weighted mean of measured concentrations.

Source: National Institute for Environment Studies Ibaraki
Reliability: (1) valid without restriction
12-AUG-2005

(28)

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Sediment Dwelling Organisms

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4.6.2 Toxicity to Terrestrial Plants

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4.6.3 Toxicity to Soil Dwelling Organisms

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4.6.4 Toxicity to other Non-Mamm. Terrestrial Species

-

4.7 Biological Effects Monitoring

-

4. Ecotoxicity

4.8 Biotransformation and Kinetics

-

4.9 Additional Remarks

-

5. Toxicity

5.0 Toxicokinetics, Metabolism and Distribution

-

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
 Species: rat
 Strain: other:Crj:CD(SD)IGS
 Sex: female
 No. of Animals: 6
 Vehicle: water

Method: other:OECD Test Guideline 423
 Year: 2004
 GLP: yes
 Test substance: other TS:KOATSU CHEMICAL INDUSTRIES, LTD., purity,99.5%
 containing 0.34% 5-methyltetrahydrofuryl alcohol as impurity.

Remark: This test was carried out based on the OECD test guideline 423, Acute Oral Toxicity - Acute Toxic Class Method. Although the starting dose level was selected 2000 mg/kg bw, no mortality was detected. Therefore, the same dose level was selected for a second step and a limit test of one dose level of 2000 mg/kg bw was carried out with six animals(three animals per step).

Result: The acute toxicity was classified on category 5 in the GHS. Clinical signs such as decreased locomotor activity and hypotonia were observed. Body weight gain and necropsy revealed no abnormality.

Source: National Institute of Health Sciences
 Reliability: (1) valid without restriction
 Flag: Critical study for SIDS endpoint
 27-APR-2005

(27)

Type: LD50
 Species: rat
 Strain: no data
 Sex: no data
 Vehicle: no data

Method: other
 Year: 1967
 GLP: no data
 Test substance: no data

Result: LD50: 1.6-3.2 g/kg
 Source: National Institute of Health Sciences
 Reliability: (4) not assignable
 27-APR-2005

(29)

5. Toxicity

Type: LD50
 Species: guinea pig
 Strain: no data
 Sex: no data
 Vehicle: no data

Method: other
 Year: 1963
 GLP: no data
 Test substance: no data

Result: LD50: 0.8-1.6 g/kg
 Source: National Institute of Health Sciences
 Reliability: (4) not assignable
 27-APR-2005

(29)

5.1.2 Acute Inhalation Toxicity

Type: LC50
 Species: rat
 Strain: no data
 Sex: no data
 Vehicle: no data
 Exposure time: 6 hour(s)

Method: other
 Year: 1963
 GLP: no data
 Test substance: no data

Result: LC50(6 hr) inhalation: 12650 ppm
 Lowest observed no effect concentration over the 6 hr
 period: 655 ppm
 Source: National Institute of Health Sciences
 Reliability: (3) invalid
 28-APR-2005

(29)

5.1.3 Acute Dermal Toxicity

Type: LD50
 Species: guinea pig
 Strain: no data
 Sex: no data
 Vehicle: no data
 Doses: no data

GLP: no data

Result: The acute dermal LD50 was less than 5 ml/kg.
 Reliability: (3) invalid
 20-MAY-2005

(29)

5. Toxicity

5.1.4 Acute Toxicity, other Routes

Type: LDLo
 Species: rat
 Strain: other: albino or Glaxo-Wistar
 Sex: male/female
 Vehicle: no data
 Route of admin.: i.p.

Year: 1959
 GLP: no data
 Test substance: no data

Remark: Number of animals: one or 3-4
 Initial test were on single animals at each dose, which were then made up to groups of 3-4 near the threshold of effects. Animals were observed for mortality and toxic effects for seven days. Survivors were killed by decapitation and examined macroscopically.

Result: Estimated approximately average lethal dose: 1000 mg/kg bw
 Estimated maximum symptomless dose: 750 mg/kg bw
 Estimated maximum dose without macroscopic pathology: 750 mg/kg bw
 Necrosis, urinary incontinence and respiratory distress were observed.

Source: National Institute of Health Sciences
 Reliability: (2) valid with restrictions
 27-APR-2005

(30)

Type: LDLo
 Species: rabbit
 Strain: no data
 Sex: no data
 Vehicle: no data
 Route of admin.: i.v.

Year: 1949
 GLP: no data
 Test substance: no data

Result: LDLo intravenous: 725 mg/kg
 Source: Research Institute for Animal Science in Biochemistry and Toxicology Sagamihara Kanagawa

Reliability: (4) not assignable
 21-DEC-2004

(20)

5. Toxicity

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: mouse
 Concentration: 100 %
 Exposure: no data
 Exposure Time: 24 hour(s)
 No. of Animals: 3
 Result: not irritating
 EC classificat.: not irritating

Method: other
 Year: 1989
 GLP: no data
 Test substance: other TS:BDH CHERMICALS, reagent grade

Remark: Strain:nude
 Sex:male
 TS was filled into a PVC cup. One cup was fastened to the dorsal side of the animals with surgical tape. TS was kept in contact with the skin for 24 h. Treated skin area was histologically examined. Three sections were selected and examined using a scoring system modified from Ingram and Grasso.
 Result: Any significant changes were not observed in histology over 24 h at 100%.
 Source: Research Institute for Animal Science in Biochemistry and Toxicology Sagamihara Kanagawa
 Test substance: other TS:BDH CHERMICALS, reagent grade.
 Reliability: (2) valid with restrictions
 13-JUN-2005 (23)

Species: human
 Result: moderately irritating
 EC classificat.: irritating

Method: other
 Year: 1989
 GLP: no
 Test substance: no data

Result: Moderate irritant to skin and mucous membranes.
 Source: Research Institute for Animal Science in Biochemistry and Toxicology Sagamihara Kanagawa
 Reliability: (3) invalid
 27-APR-2005 (4)

5. Toxicity

5.2.2 Eye Irritation

Species: rabbit
 Concentration: undiluted
 Dose: .1 ml
 Comment: not rinsed
 No. of Animals: 4
 Result: irritating
 EC classificat.: irritating

Method: Draize Test
 Year: 1977
 GLP: no data
 Test substance: no data

Remark: The test compares the subjective Draize score to several objective procedures, namely, corneal thickness measurement, evaluation of corneal and conjunctival water content, and conjunctival and aqueous humor concentrations of a dye bound to plasma proteins after intravenous injection.

After a single instillation of 0.1 mL of undiluted compound in the rabbit eye, evaluation of the above parameters was made at 2 and 24 hours. Draize score and corneal thickness were further determined daily for 10 additional days.

Result: With the modified Draize procedure, the test material was found to be irritant.

After intravenous injection, the animals were sacrificed for sampling of ocular tissues 2 hours and 24 hours after injection. The test material was found to increase the corneal thickness.

Source: Research Institute for Animal Science in Biochemistry and Toxicology Sagamihara Kanagawa

Reliability: (2) valid with restrictions
 13-JUN-2005

(15)

Species: other:NZW rabbit
 Concentration: 100 %
 Dose: .1 ml
 Comment: other: Ocular irritation recorded at 4, 24, 48, 72, 96 and 168 hr.
 No. of Animals: 6
 Result: not irritating
 EC classificat.: not irritating

Method: other: experimental protocols in European Community on dangerous substances

Year: 1988
 GLP: no data
 Test substance: other TS:Fluka A.G.,purity 99%

Remark: 100 ul of the undiluted test substance was placed into one eye of each rabbit by gently pulling the lower lid away from the eyeball to form a cup into which the test substance was dropped. The lids were then gently held together for one second and the rabbit was replaced in its cage. The other,

5. Toxicity

untreated, eye served as a control. The eyes were not washed following instillation of the test substance. The eyes were examined and the grade of ocular reaction was recorded at 4, 24, 48, 72, 96 and 186 hours. Erythema, chemosis, iritis and corneal opacity were scored according to the Draize scores. The test substance was classified according to the EEC Directive 83/467/EEC.

Result: This chemical was not irritant to the rabbit eye
 Source: Research Institute for Animal Science in Biochemistry and Toxicology Sagamihara Kanagawa
 Reliability: (2) valid with restrictions
 28-APR-2005 (21)

Species: rabbit
 Concentration: 100 %
 Dose: 20 other: mg
 Exposure Time: 24 hour(s)
 Result: irritating
 EC classificat.: irritating

Method: other
 Year: 1972
 GLP: no data
 Test substance: no data

Result: 20 mg instilled into rabbit eye(24 hr) caused moderate to severe irritation.
 Source: Research Institute for Animal Science in Biochemistry and Toxicology Sagamihara Kanagawa
 Reliability: (4) not assignable
 27-APR-2005 (26)

Species: human

Method: other
 Year: 1996
 GLP: no
 Test substance: no data

Result: A severe eye irritant.
 Source: Research Institute for Animal Science in Biochemistry and Toxicology Sagamihara Kanagawa
 Reliability: (4) not assignable
 27-APR-2005 (24)

5.3 Sensitization

-

5. Toxicity

5.4 Repeated Dose Toxicity

Species: rat Sex: male/female
 Strain: other:Crj:CD(SD)IGS
 Route of administration: gavage
 Exposure period: 28 days
 Frequency of treatment: once a day
 Post exposure period: 14 days (recovery period)
 Doses: 10, 40, 150 and 600 mg/kg bw/day
 Control Group: yes, concurrent vehicle

Method: other: Guideline for the 28-Day Repeated Dose Toxicity Test in Mammalian Species (Chemical Substances Control Law of Japan)
 Year: 2004
 GLP: yes
 Test substance: other TS:KOATSU CHEMICAL INDUSTRIES, LTD., purity,99.5% containing 0.34% 5-methyltetrahydrofuryl alcohol as impurity.

Remark: Study design:
 Vehicle: Distilled water
 Number of animals/groups: Males, 5; females, 5
 Administration period: Males and females, 28 days
 Recovery period: Males and females at doses of 0 and 600 mg/kg bw/day, 14 days
 Terminal killing: Males and females, day 29 or 43

Clinical observation and measurement:
 General conditions were observed once a day during administration and recovery periods. Detailed clinical signs in FOB(Functional Observation Batteries) were observed for all animals on day 7, 14, 21 and 28 of administration period and on day 7 and 14 of recovery period.

Sensory/reflex test:
 Responses in sensory/reflex test were determined for all animals on day 28 of administration period and on day 14 of recovery period.

Determinations of landing foot splay, grip strength and spontaneous motor activity were carried out for all animals on day 23 of administration period and on day 13 of recovery period.

Body weights were determined on day 1 (before dosing), 3, 7, 10, 14, 17, 21, 24 and 28 of administration period and on day 3, 7, 10 and 14 of recovery period.

Food consumption was determined for 24 hours at once a week of administration and recovery periods for both sexes.

Urinalysis was carried out on day 26 of administration period, on day 12 of recovery period for both sexes.

Hematological and biochemical examinations were carried out at time of necropsy after administration period and recovery periods for both sexes.

Organ weights were measured in five animals/group/sex at necropsy after administration and recovery periods.

5. Toxicity

Organ weights measured: Brain, heart, thymus, liver, kidney, spleen, adrenal, testis and epididymus in males and brain, heart, thymus, liver, kidney, spleen, adrenal and ovary in females.

Microscopic examination: Brain, pituitary, thyroid, parathyroid, thymus, heart, lung, trachea, liver, kidney, spleen, adrenal, stomach, intestine, urinary bladder, spinal cord, lymph node, sciatic nerve, bone marrow, testis, epididymus, prostate, ovary and uterus for all animals of 0 and 600 mg/kg bw/day groups killed after 28 days of administration period, thymus for both sexes, testis and spleen for males of 10, 40 and 150 mg/kg bw/day groups killed after recovery period.

Statistical methods: Dunnett's test for data of administration period, and t-test or U-test for data of recovery period and Fisher's exact test for quantal data. Significance level is 5%.

Result:

NOAEL: 40 mg/kg bw/day

NOEL: 40 mg/kg bw/day

Mortality: There was no mortality related to the test substance treatment.

Clinical signs: Increased locomotor activity followed by decreased locomotor activity and adoption of a prone position in males and females of the 600 mg/kg bw/day group. Increased locomotor activity without any other sign was observed in females of the 150 mg/kg bw/day group. Determination of grip strength: Decreased grip strength of the hindlimb was observed in males of the 600 mg/kg bw/day. No effects on sensory/reflex, landing foot splay and spontaneous motor activity were observed.

Body weight: Statistically significant suppression of body weight gain was noted in males of the 600 mg/kg bw/day group.

Food consumption: Food consumption was statistically significantly decreased throughout the administration period in males of the 600 mg/kg bw/day group. In females of the same dose group, food consumption was statistically significantly decreased only in the 1st week of the administration period.

Urinalysis: Statistically significant decreased urinary pH was detected in males of 600 mg/kg bw/day group.

At the examination of a 28-day administration period

Male

Dose(mg/kg bw/day)	0	10	40	150	600
No.of animals	10	5	5	5	10
PH	6.0	0	0	0	4
	6.5	0	0	0	1
	7.0	0	0	0	3

7.5	4	4	3	1	2**
8.0	1	1	0	0	0
8.5	5	0	2	4	0

Note: **:P<0.01

Hematology: At the examination after a 28-day administration period, statistically significant decreases in MCH, MCHC, leukocyte count and platelet count and prolongation of prothrombin time in males and females, in addition to decreases in reticulocyte count in males and hemoglobin concentration in females of the 600 mg/kg bw/day group. At the examination after a 14 recovery period, the changes observed at the examination after a 28-day administration period were not observed.

At the examination after a 28-day administration period
Male

Dose (mg/kg bw/day)		0	10	40	150	600
No.of animals		5	5	5	5	5
MCH(pg)	Mean	19.4	19.8	19.4	19.3	18.3*
	SD	0.5	0.6	0.4	0.4	0.8
MCHC(%)	Mean	33.8	33.9	33.2	33.1	32.3**
	SD	0.3	0.4	0.7	0.5	0.5
Leukocyte (10e+2/uL)	Mean	63	63	61	54	37*
	SD	15	11	16	12	9
Platelet (10e+4/uL)	Mean	152	151	159	134	87**
	SD	6	12	18	15	12
Reticulocyte (0/00)	Mean	37	42	41	30	21**
	SD	6	5	3	5	6
PT(sec)	Mean	12.9	12.8	12.7	13.2	13.9*
	SD	0.5	0.2	0.3	0.6	0.1

Note: *:P<0.05; **:P<0.01

Female

Dose (mg/kg bw/day)		0	10	40	150	600
No.of animals		5	5	5	5	5
Hemoglobin(g/dL)	Mean	15.7	15.8	15.4	15.8	14.6**
	SD	0.4	0.6	0.7	0.3	0.4
MCH(pg)	Mean	19.1	19.7	18.8	18.9	18.0*
	SD	0.3	1.2	0.5	0.4	0.5
Leukocyte (10e+2/uL)	Mean	50	52	50	40	23*
	SD	19	15	11	13	7
Platelet (10e+4/uL)	Mean	141	153	145	134	85**
	SD	22	14	9	22	15
PT(sec)	Mean	13.3	13.2	13.8	13.6	14.6**
	SD	0.6	0.3	0.6	0.2	0.6

Note: *:P<0.05; **:P<0.01

Blood biochemistry: At the examination after a 28-day administration period, statistically significant decrease of ALP, total protein, albumin, total bilirubin and calcium in males and females, and LDH, triglyceride and sodium in males of the 600 mg/kg bw/day group. Additionally, statistically

significant increase in BUN in males of the 600 mg/kg bw/day. In the 150 mg/kg bw/day, statistically significant decrease in total protein was observed in males.

At the examination after a 14 recovery period, a statistically significant decrease in calcium was observed in males and females of the 600 mg/kg bw/day.

At the examination after a 28-day administration period

Male

Dose (mg/kg bw/day)		0	10	40	150	600
No.of animals		5	5	5	5	5
LDH(IU/L)	Mean	251	421	242	186	134*
	SD	65	212	41	38	32
T.protein(g/dL)	Mean	5.89	5.74	5.77	5.51**	5.20**
	SD	0.12	0.10	0.12	0.20	0.17
Albumin(g/dL)	Mean	2.89	2.84	2.85	2.69	2.59*
	SD	0.12	0.09	0.15	0.16	0.16
Triglyceride (mg/dL)	Mean	50	61	49	28	26*
	SD	11	11	26	6	8
BUN(mg/dL)	Mean	13.0	15.6	13.5	14.8	17.0*
	SD	1.0	2.4	1.1	1.8	3.1
T. bilirubin (mg/dL)	Mean	0.34	0.32	0.34	0.30	0.25*
	SD	0.04	0.04	0.04	0.01	0.01
Ca(mg/dL)	Mean	10.2	10.0	10.1	9.9	9.7**
	SD	0.3	0.2	0.1	0.1	0.2
Na(mEq/L)	Mean	148	147	148	146	145**
	SD	1	1	1	1	1

Note: *:P<0.05; **:P<0.01

Female

Dose (mg/kg bw/day)		0	10	40	150	600
No.of animals		5	5	5	5	5
ALP(IU/L)	Mean	485	414	459	375	277**
	SD	97	144	70	56	43
T.protein(g/dL)	Mean	6.16	6.14	5.83	5.76	5.30**
	SD	0.41	0.14	0.23	0.16	0.23
Albumin(g/dL)	Mean	3.20	3.08	2.82*	3.02	2.58**
	SD	0.31	0.11	0.26	0.14	0.22
T.bilirubin (mg/dL)	Mean	0.23	0.22	0.22	0.21	0.17**
	SD	0.01	0.02	0.03	0.04	0.01
Ca(mg/dL)	Mean	10.1	9.9	9.7*	9.9	9.7*
	SD	0.3	0.1	0.0	0.2	0.0

Note: *:P<0.05; **:P<0.01

At the examination after a 14-day recovery period

Male

Dose (mg/kg bw/day)		0	600
No.of animals		5	5
Ca(mg/dL)	Mean	9.7	9.3*
	SD	0.1	0.2

Note: *:P<0.05

Female			
Dose (mg/kg bw/day)		0	600
No.of animals		5	5
Ca(mg/dL)	Mean	9.9	9.4*
	SD	0.4	0.3

Note: *:P<0.05

Necropsy: At the examination after a 28-day administration period, a small-sized thymus was observed in five males and four females of the 600 mg/kg bw/day group. At the examination after a 14-day recovery period, a small-sized thymus was observed in two males and small-sized testes were observed in three males of the 600 mg/kg bw/day group.

Organ weight

At the examination after a 28-day administration period, there were statistically significant decreases in final body weight in males, absolute and relative thymus weights in males and females and absolute and relative pituitary weights in females of the 600 mg/kg bw/day group. A statistically significant decrease in absolute weights of brain, liver, heart, pituitary, adrenals, testes and epididymides in males and increase in relative kidney weight in females were also observed in the 600 mg/kg bw/day group. In the 150 mg/kg bw/day group, a statistically significant decrease in relative pituitary weight was observed in females.

At the examination after a 14-day recovery period, statistically significant decrease in absolute and relative thymus weights in males and increase in absolute and relative thyroid weight in females, and decreases in final body weight, absolute weights of liver, kidneys, spleen, adrenals, testes and epididymides and increases in relative weight of heart and pituitary in males of the 600 mg/kg bw/day group were observed.

At the examination after a 28-day administration period

Male						
Dose (mg/kg bw/day)		0	10	40	150	600
No.of animals		5	5	5	5	5
Body weight(g)	Mean	357	348	362	326	290**
	SD	30	28	43	16	28
Absolute weight						
Brain(g)	Mean	1.94	1.87	1.99	1.82	1.77**
	SD	0.07	0.04	0.07	0.08	0.08
Liver(g)	Mean	10.11	10.24	10.32	8.76	7.32**
	SD	1.34	0.54	1.32	0.70	0.60
Heart(g)	Mean	1.24	1.24	1.21	1.15	1.04*
	SD	0.08	0.23	0.08	0.04	0.09
Thymus(g)	Mean	0.64	0.56	0.61	0.42	0.25**
	SD	0.14	0.05	0.16	0.04	0.04
Pituitary(mg)	Mean	12.6	11.8	11.8	10.8	9.1**
	SD	1.6	1.6	0.9	0.8	0.6

Adrenals(mg)	Mean	58.0	59.1	56.0	52.2	41.9**
	SD	9.6	10.1	6.6	4.9	4.0
Testes(g)	Mean	3.50	3.17	3.49	3.21	2.78**
	SD	0.33	0.28	0.33	0.20	0.24
Epididymides(g)	Mean	0.85	0.89	0.83	0.78	0.68**
	SD	0.05	0.11	0.08	0.03	0.06

Relative weight

Thymus(g%)	Mean	0.18	0.16	0.17	0.13	0.09**
	SD	0.03	0.01	0.04	0.01	0.01

Note: *:P<0.05; **:P<0.01

Female

Dose (mg/kg bw/day)		0	10	40	150	600
No.of animals		5	5	5	5	5
Absolute weight						
Thymus(g)	Mean	0.42	0.43	0.52	0.42	0.25**
	SD	0.04	0.07	0.11	0.10	0.04
Pituitary(mg)	Mean	13.2	13.6	14.0	12.1	10.3**
	SD	1.0	1.1	2.5	1.1	1.1

Relative weight

Kidney(g%)	Mean	0.78	0.76	0.79	0.80	0.87*
	SD	0.08	0.04	0.05	0.03	0.05
Thymus(g%)	Mean	0.20	0.21	0.23	0.19	0.12*
	SD	0.01	0.04	0.05	0.06	0.02
Pituitary(mg%)	Mean	6.4	6.4	6.3	5.5*	5.1*
	SD	0.7	0.3	0.8	0.4	0.4

Note: *:P<0.05; **:P<0.01

At the examination of a 14-day recovery period

Male

Dose(mg/kg bw/day)		0	600
No.of animals		5	5
Body weight(g)	Mean	420	355**
	SD	10	39

Absolute weight

Liver(g)	Mean	11.97	9.81**
	SD	0.58	1.12**
Kidney(g)	Mean	2.87	2.57**
	SD	0.05	0.15
Thymus(g)	Mean	0.50	0.34**
	SD	0.06	0.06
Adrenals(mg)	Mean	66.5	49.8**
	SD	8.5	2.7
Testes(g)	Mean	3.33	2.47**
	SD	0.12	0.52
Epididymides(g)	Mean	1.05	0.79**
	SD	0.07	0.09

Relative weight

Heart(g%)	Mean	0.33	0.37**
	SD	0.01	0.01
Thymus(g%)	Mean	0.12	0.10*

	SD	0.01	0.02
Pituitary(mg%)	Mean	2.8	3.2*
	SD	0.3	0.2

Note: *:P<0.05; **:P<0.01

Female			
Dose(mg/kg bw/day)		0	600
No.of animals		5	5

Absolute weight			
Thyroids(mg)	Mean	19.4	24.7*
	SD	2.7	3.0

Relative weight			
Thyroids(mg%)	Mean	8.2	10.3*
	SD	1.3	1.1

Note: *:P<0.05; **:P<0.01

Histopathology: At the examination after a 28-day administration period, atrophy of the thymus in males and females, and atrophy of the red pulp with decreased extramedullary hematopoiesis and inflammation of the capsule in the spleen and necrosis of seminiferous tubular epithelium in males of the 600 mg/kg bw/day group were observed.

Necrosis of the seminiferous tubular epithelium of the testes was also observed in males of the 150 mg/kg bw/day group.

Examination of the spermatogenic cycle revealed a decrease in the ratio of the spermatid to Sertoli cell counts in the 600 mg/kg bw/day group. At the examination after a 14-day recovery period, the testes showed a tendency for increase in severity of the changes. There was a decrease in the ratio of pachytene spermatocyte counts to Sertoli cell counts in addition to that of spermatid to Sertoli cell counts. The other changes observed during or at the examination after a 28-day administration period showed a tendency for recovery or complete recovery. There were no changes in females.

Incidence of histopathological findings at the examination after a 28-day administration period

Male						
Dose(mg/kg bw/day)		0	10	40	150	600
No.of animals		5	5	5	5	5
Spleen: Hematopoiesis,						
Extramedullary	- , +	0	2	1	3	5**
	++	5	3	4	2	0
Testis: Necrosis, seminiferous						
Epithelium	-	5	5	5	3	0
	+	0	0	0	2	5**
Thymus: Atrophy	-	5	5	5	5	0

5. Toxicity

date: 11-JAN-2006
Substance ID: 97-99-4

+ 0 0 0 0 5**

Female

Dose(mg/kg bw/day) 0 10 40 150 600
No.of animals 5 5 5 5 5Thymus: Atrophy - 5 5 5 5 0
+ 0 0 0 0 5**

Note: -:Negative; +:Slight; ++:Moderate; **:P<0.01

Incidence of histopathological findings at the examination
after a 14-day recovery period

Male

Dose(mg/kg bw/day) 0 600
No.of animals 5 5

Testis: Necrosis, seminiferous

Epithelium - 5 0
+ 0 5**

Note: -:Negative; +:Slight; **:P<0.01

Source: Research Institute for Animal Science in Biochemistry and
Toxicology Sagamihara Kanagawa

Reliability: (1) valid without restriction

Flag: Critical study for SIDS endpoint

16-AUG-2005

(27)

Species: rat Sex: male/female

Strain: no data

Route of administration: oral feed

Exposure period: 90 days

Frequency of treatment: feed ad libitum

Post exposure period: no

Doses: 1000, 3000 and 10000 ppm

Control Group: yes, concurrent no treatment

Method: other:no data

Year: 1991

GLP: no data

Test substance: no data

Remark: Study design: Sub-chronic Oral Toxicity in rats.
Groups of rats(15/sex/group) were provided diets which
contained 0, 1000, 3000, or 10000 ppm of the test material
for 90 days.Result: There was a slight depression in body weight gain in the
1000 ppm group and a statistically significant depression in
the 3000 and 10000 ppm groups.There was a statistically significant decrease in testes
weights in the 10000 ppm group. There was also a significant
decrease in the testes to body and testes to
brain weight ratios. Moderate testicular degeneration was
observed in 14 animals of the 10000 ppm group. These animals
exhibited complete loss of spermatogenic activity and their
seminiferous tubules were partially to completely lined with
a single layer of Sertoli cells. Tubules were also reduced

5. Toxicity

in size.

Source: Research Institute for Animal Science in Biochemistry and
Toxicology Sagamihara Kanagawa

Reliability: (2) valid with restrictions
27-APR-2005 (37)

Species: dog Sex: male/female
Strain: Beagle
Route of administration: oral feed
Exposure period: 90 days
Frequency of treatment: feed ad libitum
Post exposure period: no
Doses: 1000, 3000 and 6000 ppm
Control Group: yes, concurrent no treatment

Method: other:no data
Year: 1991
GLP: no data
Test substance: no data

Remark: Study design: Sub-chronic oral toxicity in dogs.
Groups of beagle dogs (4/sex/group) were provided diets
which contained 0, 1000, 3000, or 6000 ppm of the test
material for 90 days.

Result: There was a significant reduction in the body weight gains
of 2 male and female animals in the 6000 ppm group. However,
the submitter stated "it is difficult to conclude if this is
truly a test related effect, since the animals were housed
together in groups of four throughout the study. When dogs
are group housed, generally one or two animals will dominate
the others; thus limiting the intake of water and food of
the non-aggressive animals."
Testes weights of males in all treated groups were
significantly lower than controls. Severe testicular atrophy
was reported in all males at the dosage level of 6000 ppm.
Decreased spermatogenic activity was noted at 3000 ppm and
interpreted as a prodromal sign of atrophy.
There was occasional prostatic atrophy in the 6000 ppm
group. The submitter stated "it is difficult to conclude
whether or not the lower testes weights and atrophy are a
result of test compound administration or sexually immature
dogs. Because it appears randomization was not done and
therefore the larger, older male dogs were assigned to the
untreated control group, it is believed these findings in
the group males are associated with sexual immaturity."

Source: Research Institute for Animal Science in Biochemistry and
Toxicology Sagamihara Kanagawa

Reliability: (2) valid with restrictions
27-APR-2005 (37)

5. Toxicity

Species: dog Sex: male
 Strain: Beagle
 Route of administration: oral feed
 Exposure period: 90 days
 Frequency of treatment: feed ad libitum
 Post exposure period: no
 Doses: 200, 400 and 800 ppm
 Control Group: yes, concurrent no treatment

Method: other
 Year: 1991
 GLP: no data
 Test substance: no data

Remark: Study design: Sub-chronic testicular maturation study in dogs.
 Groups of 4 male beagle dogs were provided with diets containing 0, 200, 400, or 800 ppm of the test material for 90 days.

Result: One animal each at 200 and 400 ppm groups exhibited lower testes weights and testes to body weight ratios than controls. Also, these two animals had relatively little to no spermatogenesis. Sexual immaturity was reported as the probable cause for these findings. However, since no clear-cut dose correlation was observed and animals at 800 ppm exhibited normal testicular development, these depressions were not reported as significant.

Source: Research Institute for Animal Science in Biochemistry and Toxicology Sagamihara Kanagawa

Reliability: (2) valid with restrictions
 27-APR-2005 (37)

Species: rat Sex: male/female
 Strain: no data
 Route of administration: oral feed
 Exposure period: 90 days
 Frequency of treatment: feed ad libitum
 Post exposure period: no
 Doses: 500, 1000, 5000 and 10000 ppm
 Control Group: yes, concurrent no treatment

Method: other
 Year: 1991
 GLP: no data
 Test substance: no data

Remark: Study design: Sub-chronic dietary toxicity study in rats.
 Groups of rats (20/sex/group) were provided with diets containing 0, 500, 1000, 5000, or 10000 ppm of the test material for 90 days.

Result: A statistically significant depression in mean body weight gains was noted in male rats in the 5000 and 10000 ppm groups during weeks 1-13. Male rats in the 1000 ppm group showed a statistically significant depression in mean body weight gains for study weeks 5, 6, 7 and 8-13.

5. Toxicity

Females in the 10000 ppm group had a statistically significantly depressed mean body weight gains during study weeks 8-13.

The mean weights of brain, kidneys, liver, seminal vesicles, epididymides, prostate, testes and adrenal glands were all statistically significantly decreased for male rats in the 10000 ppm group. Except for kidneys, the same observation was noted for males in the 5000 ppm group. Only the brain and liver, and liver mean weights of males in the 1000 and 500 ppm groups, respectively, were statistically significantly decreased. The females in the 10000 ppm group showed only a significant decrease in mean brain weight. The mean brain and kidney to final body weight ratios were statistically significantly increased for males in the 5000 ppm and 10000 ppm groups. Mean liver to final body weight ratios were decreased in males in all treated groups. Other statistically significant decreases in males for mean relative organ weights were epididymides, and testes at the dosage levels of 5000 to 10000 ppm, and 10000 ppm respectively. The mean kidneys; liver; and ovaries to final body weight ratios were statistically significantly increased for females in the 5000, 5000 and 10000, and 10000 ppm groups, respectively.

There were significant decreases in the glucose, total protein, globulin and calcium at dosage levels of 1000, 5000, and 10000 ppm at 13 weeks in the males. In the females, there were significant decreases in the hemoglobin, MCV, MCH, MCHC, and platelets.

Source: Research Institute for Animal Science in Biochemistry and Toxicology Sagamihara Kanagawa

Reliability: (2) valid with restrictions
27-APR-2005

(33)

Species: rabbit Sex: female
Strain: no data
Route of administration: gavage
Exposure period: 5 days
Frequency of treatment: once aday
Post exposure period: no
Doses: 30, 100, 300 and 1000 mg/kg bw/day
Control Group: yes

Method: other
Year: 1991
GLP: no data
Test substance: no data

Remark: Study design: Sub-acute oral toxicity study in rabbits. The test material was administered to groups of three female rabbits at dosage levels of 0, 30, 100, 300, or 1000 mg/kg bw/day for five days.

Result: Two of the animals in the 1000 mg/kg bw/day group were sacrificed moribund after receiving one dose. The remaining animals in the group died on study day 2. Animals in the 100 and 300 mg/kg bw/day groups elected not

to eat after receiving their first dose of the test material. In the 30 mg/kg bw/day group, diet consumption ceased after receiving the fourth dose. Mean body weight gain decreased 6.3%, 7.3%, and 8.5% for the 30, 100, and 300 mg/kg bw/day groups, respectively. Clinical signs seen in one or two animals from the 300 and 1000 mg/kg bw/day groups included decreased motor activity, unsteady walk, and prostration. Two animals in the 1000 mg/kg bw/day group had labored respirations.

Other clinical observations were either dried brown matting of the anogenital area, and/or wet yellow, dried tan or wet brown staining of the urogenital or anogenital area.

Necropsy of the 1000 mg/kg bw/day group revealed dark red areas

on the lungs and red foci of the stomach.

Source: Research Institute for Animal Science in Biochemistry and Toxicology Sagamihara Kanagawa

Reliability: (2) valid with restrictions

27-APR-2005

(34)

Species: rat Sex: male/female

Strain: no data

Route of administration: dermal

Exposure period: for 13 weeks

Frequency of treatment: five a week

Post exposure period: no

Doses: 100, 300, 1000mg/kg bw/day

Control Group: yes

Method: other

Year: 1995

GLP: no data

Remark: The test material was administered dermally the dorsal regions of male and female rats at the dosages of either 100, 300, or 1000mg/kg bw/day, five a week for at least 65 applications. The study was designed whereby the number of animals being evaluated was 17 males and 12 females per group. After seven weeks on study, five males from each group were randomly selected for termination as required by a specific section of the protocol for an interim evaluation of reproductive tissue. The remaining 24 animals per group were terminated after 13 weeks.

Result: No treatment-related effects with respect to survival, clinical observations, ophthalmic examinations, hematology values and serum chemistries, absolute and relative organ weights, or food consumption were observed. However, statistically significant decreases in weekly body weights were noted at 5% level of probability for week 9 through 12 and at 1% level of probability for week 13 in the high dose males (1000mg/kg bw/day).

Reliability: (2) valid with restrictions

13-JUN-2005

(32)

5. Toxicity

Species: rat Sex: male/female
 Strain: no data
 Route of administration: inhalation
 Exposure period: 90 days
 Frequency of treatment: 6 hours per day, five per week
 Post exposure period: no
 Doses: 50, 150, or 500 ppm
 Control Group: yes

Method: other
 Year: 1995
 GLP: no data
 Test substance: no data

Remark: The test material administration was by inhalation using male and female rats. Concentrations being administered were at either 50, 150, or 500 ppm, 6 hours per day, five days a week for at least 65 exposures. The study was designed whereby the number of animals being evaluated was 14 males and 10 females per group. After six weeks on study, four males from each group were randomly selected for termination as required by a specific section of the protocol for an interim evaluation of reproductive tissue. The remaining 20 animals per group were terminated after 13 weeks on study.

Result: Clinical observation: Hypoactivity and intermittent whole spasms were observed in both sexes. The spasms were concentration-related. At one-hour post-exposure, hypoactivity ceased and intermittent whole spasms became less noticeable. However, hyperactivity was noted instead and was being noted in both sexes at 500 ppm during the one-hour post-exposure observation period. Statistically significant decreases in weekly body weights were noted beginning study week one in the high concentration males(500 ppm). Significant difference from the control group was at 1% level of probability for week one through four and seven through 11, at 5% level of probability for weeks five and six. In the case of the high concentration females, statistically significant increases in weekly body weights were recorded during weeks three through nine. However, body weight gains, overall, did not reveal significant changes in either sex. Although statistically significant decreases in weekly food consumption were noted in the high concentration males, the decreases were minimal and sporadic. At four week into the study, the platelet count was statistically significantly decreased (5% level of probability) at 150 and 500 ppm in both sexes. This affect appeared to be concentration related at this time in the study. The only serum chemistry parameters related to treatment was significant increases in chloride and sodium values in males at 150 and 500 ppm.

Reliability: (2) valid with restrictions
 16-AUG-2005

(32)

5. Toxicity

Species: rat Sex: male/female
 Strain: no data
 Route of administration: inhalation
 Exposure period: 90 days
 Frequency of treatment: 6 hours per day, five per week
 Post exposure period: no
 Doses: 50, 150, or 500 ppm
 Control Group: other:filtered air

Method: other
 Year: 1995
 GLP: no data
 Test substance: no data

Remark: The test material was administered via whole body inhalation to three test groups, each comprised of 14 male and 10 female rats. Exposures were for six hours per day, five days per week, for 13 weeks (at least 65 exposures). Exposure concentrations were 50, 150, and 500 ppm. After 34 exposures four males per group were terminated for assessment of spermatogenic endpoints. The remaining 10 animals per sex per group were terminated following 65 exposures (13 weeks on study). The animals were observed for clinical signs of toxicity and effects on body weight, food consumption, and clinical pathology parameters. Spermatogenic endpoints were evaluated for all males. Necropsies were performed on all animals and selected organs were weighed. A microscopic examination was conducted on selected tissues from all animals at the terminal necropsy.

Result: All animals survived to the scheduled necropsies, except for one female animals (50 ppm) that expired during the first week of exposure due to finding unrelated to the test material exposure. The predominant clinical finding was intermittent whole-body spasma, which were observed frequently, in a dose-related manner in all exposed groups. Occasional incidences of hypoactivity and excessive grooming were observed for a few animals of each sex in the high exposure group. One-hour post-exposure clinical examinations revealed hyperactivity in a dose-related manner in all test groups. Wet yellow urogenital matting and a low incidence of salivation were noted in the high exposure group, as well. Mean body weight gains in the high exposure group males decreased several times throughout the study and, therefore, resulted in decreased mean body weights, as well. Results were similarly noted in the mid-exposure group males beginning study week eight. At the end of study week 13, mean body weights in both the mid-and high-exposure group males were 9.2 and 13.3% lower, respectively, than the control group male value. In addition, mean food consumption in both the mid-and high-exposure group males was lower than the control group males throughout the study. Test females revealed body weight and food consumption means that were similar to those of the control group females values. Test material related changes in hematology parameters

5. Toxicity

consisted of decreased platelet and hemoglobin means in the high exposure group males and females at study weeks three and 13. Also a decrease in MCH values was noted in the high exposure group males at study week three and in the high exposure group males and females at study week 13. At both study weeks six and 13 (interim and terminal necropsied, respectively), decreased incidence of morphologically abnormal sperm were observed in the high exposure group males. Mean absolute and relative prostate weights were decreased in both the mid- and high-exposure groups. Mean absolute seminal vesicle weight, and absolute and relative epididymides weights were also decreased in the high exposure group males. The only microscopic lesion suggestive of a test material related effect was mild multifocal atrophy of the testes in a single high exposure group male.

Based on the data obtained, NOEL could not be established via whole body inhalation after 13 weeks of exposure.

Reliability:
13-JUN-2005

(2) valid with restrictions

(35)

Species: rat Sex: male/female
Strain: no data
Route of administration: dermal
Exposure period: 90 days
Frequency of treatment: five days per week
Post exposure period: no
Doses: 100, 300, 1000 mg/kg bw/day
Control Group: yes, concurrent vehicle

Method: other
Year: 1995
GLP: no data
Test substance: no data

Remark: Each groups consisted of 17 males and 12 females. The test substance was administered undiluted five days per week for 13 consecutive weeks for at least 65 applications to shaved intact dorsal skin. Application sites were wrapped for six hours using an occlusive wrap/binder. Selected dosage levels were 100, 300, and 1000 mg/kg bw/day. A concurrent control group of identical design received 0.9% saline on a comparable regiment at a dose volume (0.95 mL/kg) equivalent to the highest dose level. After 37 applications, five males per group were terminated from the study for assessment of spermatogenic endpoints. The remaining 12 animals per sex per group were terminated following 13 weeks of study (65 applications). All animals were observed for signs of overt toxicity, dermal irritation, effects on body weight, food consumption, and hematology and serum chemistry parameters. Spermatogenic endpoints were evaluated for all males. Complete necropsies were performed on all animals and selected organs were weighed. Microscopic examination was conducted on selected tissues from all animals terminated at 13 weeks.

5. Toxicity

Result: There were no mortality in the study.
No test substance related clinical signs were observed at any dose level and only very limited dorsal irritation occurred. Mean food consumption and hematology and serum chemistry parameters were unaffected by test substance treatment. In addition, no test substance related macroscopic or microscopic lesions were observed. Organ weights were unaffected by the dorsal application as well.

Mean body weights and body weight gains resulted in both males and females at the dose level of 1000 mg/kg bw/day. Also, an adverse effect on spermatogenesis was noted following 13 consecutive weeks of test substance administration. The mean number of sperm in the testis and the mean sperm production rate were decreased in both the 300 and 1000 mg/kg bw/day group males. In addition, a decrease in the mean percentage of motile sperm was noted in the 1000 mg/kg bw/day group males. No histopathological lesions were observed in the testis, epididymis, seminal vesicles, vas deferens, prostate, or coagulating gland.

Reliability: (2) valid with restrictions
13-JUN-2005

(36)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Test species/strain :Salmonella typhimurium TA100, TA1535, TA98, TA1537, Escherichia coli WP2 uvrA/pKM101
Concentration: 0, 313, 625, 1250, 2500, 5000 ug/plate(all strains)
Cytotoxic Concentration: The chemical did not induce cytotoxicity.
Metabolic activation: with and without
Result: negative

Method: other: Guideline for Screening Mutagenicity Testing of Chemicals(Chemical Substances Control Law of Japan) and OECD Test Guideline 471
Year: 2004
GLP: yes
Test substance: other TS:KOATSU CHEMICAL INDUSTRIES, LTD., purity,99.5% containing 0.34% 5-methyltetrahydrofuryl alcohol as impurity.

Remark: Solvent:Water for injection
Procedures: Pre-incubation method
Dosage of each strain with or without S9
-S9 mix:0, 313, 625, 1250, 2500, 5000 ug/plate(TA100, TA1535, TA98, TA1537, WP2 uvrA/pKM101)
+S9 mix:0, 313, 625, 1250, 2500, 5000 ug/plate(TA100, TA1535, TA98, TA1537, WP2 uvrA/pKM101)
S9:Rat liver, induced with phenobarbital and 5,6-benzoflavone
Positive control:
-S9 mix; 2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide (TA100, TA98), Sodium azide (TA1535) and 9-Aminoacridine hydrochloride (TA1537) and

N-Ethyl-N'-nitro-N-nitro-soguanidine (WP2uvrA/pKM101)
+S9 mix; 2-Aminoanthracene (all strains)
Plates/test:3
Number of replicates:2

Result: There were no precipitation in any test concentration.
Cytotoxic concentration: Growth inhibition was not observed
up to 5000 ug/plate for any stains, with or without S9 mix.
Genotoxic effects:
Positive control:
With metabolic activation: positive
Without metabolic activation: positive

Salmonella typhimurium TA100, TA98, TA1535, TA1537
With metabolic activation: negative
Without metabolic activation: negative

Escherichia coli WP2 uvrA/pK101
With metabolic activation: negative
Without metabolic activation: negative

Source: Research Institute for Animal Science in Biochemistry and
Toxicology Sagamihara Kanagawa

Reliability: (1) valid without restriction

Flag: Critical study for SIDS endpoint

26-APR-2005 (27)

Type: Chromosomal aberration test
System of testing: Type of cell used: Chinese hamster lung(CHL/IU) cells
Concentration: 257.5, 515, 1030 ug/mL
Metabolic activation: with and without
Result: negative

Method: other:Guideline for Screening Mutagenicity Testing of
Chemicals(Chemical Substances Control Law of Japan) and OECD
Test Guideline 473

Year: 2004
GLP: yes

Test substance: other TS:KOATSU CHEMICAL INDUSTRIES, LTD., purity,99.5%
containing 0.34% 5-methyltetrahydrofuryl alcohol as impurity.

Remark: Solvent: Isotonic sodium chloride solution
S9: Rat liver, induced with phenobarbital and
5,6-benzoflavone
Positive control: Cyclophosphamide (with S9), Mitomycin C
(without S9)
Plates/test: 2
The maximum concentration was established, based on the
growth inhibition test. In this test, growth inhibition
was not observed at concentration of 1030 ug/mL (10 mmol/L)
with or without S9 mix.
Dosage:
-S9 mix(6 hr short-term treatment):257.5, 515, 1030 ug/mL
+S9 mix(6 hr short-term treatment):257.5, 515, 1030 ug/mL
-S9 mix(24 hr continuous treatment):257.5, 515, 1030 ug/mL

Result: The chemical did not induce structural chromosomal
aberrations or polyploidy under the conditions of this

5. Toxicity

experiment.

Genotoxic effects:

	clastogenicity			polyploidy		
	+	?	-	+	?	-
Without metabolic activation:	[]	[]	[*]	[]	[]	[*]
With metabolic activation:	[]	[]	[*]	[]	[]	[*]

	clastogenicity			polyploidy		
	+	?	-	+	?	-
Positive control						
Without metabolic activation:	[*]	[]	[]	[]	[]	[*]
With metabolic activation:	[*]	[]	[]	[]	[]	[*]

Source: Research Institute for Animal Science in Biochemistry and Toxicology Sagamihara Kanagawa

Reliability: (1) valid without restriction

Flag: Critical study for SIDS endpoint

16-AUG-2005

(27)

5.6 Genetic Toxicity 'in Vivo'

-

5.7 Carcinogenicity

-

5.8.1 Toxicity to Fertility

Type: other:Preliminary Reproduction Toxicity Screening Test

Species: rat

Sex: male/female

Strain: other:Crj:CD(SD)IGS

Route of administration: gavage

Exposure Period: 47 days for males; 42-52 days from 14 days before mating to 4 days after delivering for females

Frequency of treatment: once a day

Premating Exposure Period

 male: 14 days

 female: 14 days

Duration of test: 47 days for males; 42-52 days for females

Doses: 15, 50, 150, 500 mg/kg bw/day

Control Group: yes, concurrent vehicle

Method: other:OECD Test Guideline 421

Year: 2004

GLP: yes

Test substance: other TS:KOATSU CHEMICAL INDUSTRIES, LTD., purity,99.5% containing 0.34% 5-methyltetrahydrofuryl alcohol as impurity.

Remark: Study design:
 Vehicle: Distilled water
 Terminal killing: Males, day 47; females, day 4 of lactation

Clinical observation performed and frequency: General condition was observed once a day, body weights were determined once a week during treatment period for males and once a week before mating and on day 0, 7, 14 and 20 of gestation period and on day 0 and 4 of lactation period for females, food consumption was determined once a week during treatment period for males and once a week before mating and on day 0,7,14 and 20 of gestation period and on day 0 and 4 of lactation for females.

For all males and all females after parturition, necropsy was carried out after 48 days for males and at 5 days after delivery for females.

Organ weights measured: Kidneys, thymus and pituitary for both sexes, and testes and epididymides for males. In males, the organs were weighed in all animals survived; 12 animals in the 0, 50, 150 and 500 mg/kg bw/day groups and in 11 males in 15 mg/kg bw/day group. In females, the organs were weighed in all pregnant rats with parturition; 12 animals in the 0 and 50 mg/kg bw/day groups, in 10 animals in 15 mg/kg bw/day group and in 9 animals in 150 mg/kg bw/day group. In the 500 mg/kg bw/day group, all animals did not delivery.

Microscopic examination: Pituitary, thymus, testes and epididymides for 12 males and pituitary, thymus and ovary for 12 females in 0 and 5000 mg/kg bw/day groups, and spleen for 5 males and females in 0, 15, 50 and 150 mg/kgbw/day groups and 12 males and females in 500 mg/kg bw/day group. Additionally, the dead male in the 15 mg/kg bw/day group was examined for testis, epididymis, pituitary, brain, spinal cord, stomach, intestine, adrenal, spleen, heart, liver, kidney, thyroid, trachea, lung, urinary bladder, sciatic nerve, bone marrow and lymph node. Each one no-pregnant female in the 15 and 150 mg/kg bw/day groups and the one female paired with the dead male in the 15 me/kg bw/day group examined for ovary, uterus and pituitary. The two males without fertility in the 15 and 150 mg/kg bw/day groups were examined for testis, epididymis, prostate and seminal vesicle.

Reproductive and developmental parameters: Estrous cycle, no.of successful copulation, copulation index, paring days until copulation, no.of pregnant females, fertility index, no.of corpora lutea, no.of implantation sites, implantation index[(no.of implantations/no.of corpora lutea)x100], no.of pregnant females with parturition, gestation length, no.of pregnant females with live pups, gestation index[(no.of dam with live newborns/no.of pregnant females)x100], and no.of pregnant females with live pups on day 4, no.of pups born, delivery index, no.of pups alive on day 0 of lactation, live birth index[(no.of live newborns/no.of implantations)x100], sex ratio, no.of pups alive on day 4 of lactation, viability index[(no.of live newborns on day 4 after birth/no.of live newborns)x100], body weight of live pups.

5. Toxicity

no.of external anomalies and internal variations.

Statistical methods: Dunnett's or Scheffe's test for continuous data, Chi square test for reproductive parameters, and Fischer's exact test for pathological findings.

Result: NOAEL: 50 mg/kg bw/day for repeated dose toxicity of males and females, 150 mg/kg bw/day for parent males and 50 mg/kg bw/day for parent females in reproductive performance and 50 mg/kg bw/day for offspring development.

Mortality: There was no mortality related to the test material treatment.

Clinical signs, body weight and food consumption: Increased locomotor activity or increased locomotor activity followed by decreased locomotor activity was observed in males and females of the 150 and 500 mg/kg bw/day groups. Suppression of body weight gain in males at 500 mg/kg bw/day and in females at 150 mg bw/day and higher, and decreased food consumption in males and females at 150 mg/kg bw/day and higher were also noted.

Necropsy:

Male: A small-sized testis and epididymis were observed in one in the 0, 15 and 150 mg/kg bw/day groups and ten in the 500 mg/kg bw/day group. In spleen, rough of surface was observed in six in the 500 mg/kg bw/day group, and white spot/area in the surface was observed in one in the 150 mg/kg bw/day group and four in the 500 mg/kg bw/day group.

Female: A small-sized thymus was observed in five, and rough of surface and white spot/area in the surface in spleen was observed in eleven and five, respectively, in the 500 mg/kg bw/day group. In two females in the 150 mg/kg bw/day group and twelve females in the 500 mg/kg bw/day group with embryonic death, early/late resorption of embryo was observed.

Organ weights: Statistically significant decreases in body weight, absolute weights of kidneys, thymus, pituitary, testes and epididymides, and relative weight of thymus, testes and epididymides in males in the 500 mg/kg bw/day group and absolute pituitary weight in the 150 mg/kg bw/day group were detected. Statistically significant decreases in body weight and absolute pituitary weight and increase in relative kidney weight in females in the 150 mg/kg bw/day group were detected.

Males:

Dose(mg/kg bw/day)	0	15	50	150	500
No.of animals	12	11	12	12	12

Body weight(g)	Mean	550	535	538	517	489**
	SD	40	30	28	22	33

Absolute:

Kidneys(g)	Mean	3.10	3.15	3.09	2.90	2.71**
------------	------	------	------	------	------	--------

	SD	0.18	0.32	0.20	0.20	0.20
Thymus(g)	Mean	0.36	0.32	0.35	0.31	0.19**
	SD	0.07	0.06	0.06	0.07	0.05
Pituitary(mg)	Mean	15.6	15.6	14.2	13.4*	12.2**
	SD	1.5	2.0	1.3	1.5	1.2
Testes(g)	Mean	3.41	3.18	3.52	3.40	1.77**
	SD	0.50	0.83	0.29	0.45	0.44
Epididymides(g)	Mean	1.40	1.30	1.38	1.26	0.87**
	SD	0.20	0.30	0.15	0.17	0.15
Relative:						
Thymus(g%)	Mean	0.07	0.06	0.07	0.06	0.04**
	SD	0.01	0.01	0.01	0.01	0.01
Testes(g%)	Mean	0.63	0.60	0.66	0.66	0.36**
	SD	0.11	0.15	0.07	0.10	0.09
Epididymides (g%)	Mean	0.26	0.24	0.26	0.24	0.18**
	SD	0.04	0.05	0.03	0.04	0.03
Female						
Dose(mg/kg)		0	15	50	150	500
No.of animals		12	10	12	9	0
Body weight(g)	Mean	363	350	339	313	-
	SD	25	35	24	27**	
Absolute:						
Pituitary(mg)	Mean	20.1	18.3	17.6	16.0*	-
	SD	3.8	1.7	1.8	1.9	
Relative:						
Kidneys(g%)	Mean	0.57	0.57	0.61	0.63*	-
	SD	0.04	0.06	0.05	0.05	

Note: *:P<0.05; **:P<0.01

Microscopic examination: There were atrophy of the thymus in both sexes and atrophy of the seminiferous tubule with hyperplasia of the interstitial cell in the testes and decreased intraluminal sperm with cell debris in the epididymides of the 500 mg/kg bw/day group. Atrophy of the red pulp with decreased extramedullary hematopoiesis in the spleen in the 150 and 500 mg/kg bw/day groups, and inflammation of the spleen capsule in the 500 mg/kg bw/day group were also observed in both sexes.

Incidence of histopathological findings

Male

Dose(mg/kg bw/day)		0	15	50	150	500
Thymus: Atrophy	-	12	5	5	4	3
	+,++,+++	0	0	0	1	9**
		(12)	(5)	(5)	(5)	(12)
Testis: Atrophy, seminiferous tubule	-	11	5	5	4	0
	+,++,+++	1	0	0	1	12**
		(12)	(5)	(5)	(5)	(12)
Hyperplasia, interstitial cell						

	-	11	5	5	5	2
	+,++	1	0	0	0	10**
		(12)	(5)	(5)	(5)	(12)
Epididymides: Decrease, sperm						
	-	11	5	5	4	0
	+,++,+++	1	0	0	1	12**
		(12)	(5)	(5)	(5)	(12)
Cell debris, lumen						
	-	11	5	5	4	0
	+,++	1	0	0	1	12**
		(12)	(5)	(5)	(5)	(12)
Spleen: Inflammation, capsule						
	-	5	5	5	2	1
	+,++,+++	0	0	0	3	11**
		(5)	(5)	(5)	(5)	(12)

Note:(n):No.of animals examined.
 - :Negative; +:Slight; ++:Moderate; +++:Severe
 **:P<0.01

Female
 Dose(mg/kg bw/day) 0 15 50 150 500

Spleen: Hematopiesis, extramedullary						
	-,+	0	0	1	5	11
	++,+++	5	5	4	0**	1**
		(5)	(5)	(5)	(5)	(12)
Inflammation, capsule						
	-	5	5	5	3	0
	+,++,+++	0	0	0	2	12**
		(5)	(5)	(5)	(5)	(12)

Note:
 (n):No.of animals examined.
 - :Negative; +:Slight; ++:Moderate; +++:Severe
 **:P<0.01

Reproductive and developmental parameters: Prolongation of gestation length and lowering of the gestation index in female parents, and decreases in numbers of born pups and live pups on day 0 of lactation and indexes for delivery, live birth and viability were observed in the 150 mg/kg bw/day group. In the 500 mg/kg bw/day group, no females delivered because of early resorptions of embryos. No increases in the incidence of fetuses with external and internal abnormalities were detected in pups of any dose groups.

Reproduction results:					
Dose(mg/kg bw/day)		0	15	50	150 500
No.of pairs mated		12	12	12	12 12
Estrous cycle(days) Mean		4.3	4.0	4.1	4.5 4.8*
SD		0.6	0.1	0.3	0.6 0.5
No.of pairs with successful copulation		12	11	12	12 12

Copulation index(%)		100	91.7	100	100	100
Pairing days until copulation(day)	Mean	2.7	2.5	2.9	2.3	3.7
	SD	1.2	1.4	1.2	1.4	2.7
No.of pregnant females		12	10	12	11	12
Fertility index(%)		100	90.9	100	91.7	100
No.of corpora lutea	Mean	17.7	16.5	17.8	16.4	17.0
	SD	2.1	2.7	1.5	2.0	2.8
No.of implantation sites	Mean	15.6	15.3	16.1	13.7	14.5
	SD	1.3	1.9	1.8	2.1	3.7
Implantation index(%)	Mean	88.8	93.5	90.7	84.5	87.9
	SD	7.4	7.4	8.0	13.1	23.7
No.of pregnant females with parturition		12	10	12	9	0
Gestation length(days)	Mean	22.6	22.7	22.9	24.0**	-
	SD	0.5	0.5	0.3	0.0	-
No.of pregnant females with live pups		12	10	12	4	-
Gestation index(%)		100	100	100	36.4**	-
No.of pregnant females with live pups on day 4		12	10	12	1	-

Note:**:P<0.05; ***:P<0.01

Litter results:

Dose(mg/kg bw/day)		0	15	50	150	500
No.of pups born	Mean	14.8	14.5	14.8	7.0**	-
	SD	1.6	2.1	1.7	1.4	-
Delivery index(%)	Mean	95.3	94.7	91.9	46.4*	-
	SD	7.1	6.2	5.9	14.0	-
No.of pups alive on day 0 of lactation						
Total	Mean	14.8	14.5	14.6	3.0**	-
	SD	1.6	2.1	1.8	2.2	-
Male	Mean	7.2	7.2	6.8	1.5**	-
	SD	2.1	1.9	2.5	1.7	-
Female	Mean	7.7	7.3	7.8	1.5**	-
	SD	1.8	1.6	3.0	1.9	-
Live birth index (%)	Mean	100	100	98.8	43.1*	-
	SD	0	0	2.8	29.3	-
Sex ratio(Male/Female)		0.93	0.99	0.90	1.15	-
No.of pups alive on day 4 of lactation						
Total	Mean	14.7	14.4	14.3	1.3**	-
	SD	1.6	2.1	2.0	2.3	-
Male	Mean	7.0	7.2	6.7	0.7**	-
	SD	2.3	1.9	2.7	1.2	-
Female	Mean	7.7	7.2	7.6	0.7**	-
	SD	1.8	1.7	3.1	1.2	-
Viability index (%)	Mean	98.9	99.3	97.7	26.7	-
	SD	2.6	2.1	3.5	46.2	-
Body weight of live pups(g)						

5. Toxicity

specifically in the two highest dose levels. The onset of decreased food consumption was observed first during gestation day seven and such observations continued for the most part throughout the remainder of the study.

Clinical findings associated with oral administration of 1000 mg/kg bw/day were described as impaired mobility, decreased muscle tone of hindlimbs, absence of pain response of hindlimbs, and exophthalmus of both eyes. Transient clinical findings included lacrimation of eyes, dried red material around one eye, and/or dried red material around nose.

Mean body weights per litter for both male and female fetuses at 100 mg/kg bw/day were statistically significantly lower($p < 0.01$) when compared to the control group. Although not significant statistically, 5 of 124 fetuses(4 of 8 litters) at 100 mg/kg bw/day exhibited an external malformation known as filamentous tail.

Reliability: (2) valid with restrictions
17-NOV-2005

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5.8.3 Toxicity to Reproduction, Other Studies

-

5.9 Specific Investigations

-

5.10 Exposure Experience

-

5.11 Additional Remarks

Type: other:

Remark: This study was undertaken to study the antagonistic effects of 2-furanmethanol, tetrahydro- (THFA) on induced digitalis toxicity in dogs. Experiments in dogs were divided into four categories. Those in the initial study were used for the establishment of levels of digitalis toxicity. Those in the second study received digoxin to excess and then were treated with THFA. Those in the third study received THFA alone. Finally the fourth study included animals that were pretreated with THFA and then were given digoxin to excess. For the results of THFA toxicity, each dog received a tenth of mg/kg of digoxin and then an additional 0.1 mg every 10 to 15 minutes until the criterion for digitalis toxicity was met. THFA was added so that each dog received 500 mg/kg bw, intravenously over a 5- to 10-minute period in the second study included 4 animals. In none of the 4 dogs was there recovery of sinus rhythm. Within 12 hours all dogs had expired. The third study included 3 dogs each of whom received THFA at a concentration of 500 mg/kg bw. The all animals were dead within 12 hours. In the fourth study, 2 dogs were pretreated with THFA at a concentration of 500 mg/kg bw and then made toxic with digoxin, 0.1 mg/kg. There was no obvious benefit in correction of the resulting arrhythmia, nor did the dogs survive 24 hours.

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(31)

Type: Cytotoxicity

Remark: The cellular protein content measured in cultured Hep G2 cells was used as the endpoint for determining the cytotoxicity of a range of 114 chemical compounds. The relative toxicity of the test compounds was quantified by the determination of the PI50, which is the concentration of xenobiotic required to produce a 50% reduction in protein content of the culture after 24 hr. Surfactants and heavy metals consistently had low PI50 (ex. Benzalkonium chloride, 0.003mM; Sodium dodecyl sulphate, 0.018mM; Tween 20, 1.2mM; Tween 80, 1.3mM; Cadmium chloride, 0.019mM; Mercuric chloride, 0.087mM. The PI50 of 2-furanmethanol, tetrahydro- was 178.

04-JUL-2005

(18)

Type: other

Remark: The effect of adding solvents to the pre-incubation mixture in the Salmonella/mammalian microsome assay was examined in tests of the tryptophan-pyrollysate mutagens, 3-amino-1,4-dimethyl-5H-pyrido[4,3-b]indole (Trp-P-1) and 3-amino-1-methyl-5H-pyrido[4,3-b]indole (Trp-P-2). The mutagenicity assay was carried out by using the Ames

test system with the pre-incubation modification. The strain of Salmonella was TA98. S9 was obtained from livers of SD rats induced with polychlorinated biphenyl. The pre-incubation mixture was prepared by mixing the components in the following order: the solvent to be tested; 500 uL of S9 mix; 100 uL of bacterial culture; and 25 uL of a mutagen solution. After the pre-incubation for 20 min. at 37 degree C, soft agar was added and the mixtures were poured onto the minimal agar plates. The plates were incubated for 48 h, and the revertant colonies were counted. The ratio of the number of His+ revertants found in the presence of 2-furanmethanol, tetrahydro-(THFA) to that found in the absence of solvent(control) was 5.8-5.9 adding 25 uL of THFA or 3.1-4.5 adding 50 uL of THFA. Adding 75 uL of THFA caused to kill the bacteria. Therefore, THFA showed enhancing mutagenic activity of Trp-P-1.

27-APR-2005

(1)

6.1 Analytical Methods

-

6.2 Detection and Identification

-

7.1 Function

-

7.2 Effects on Organisms to be Controlled

-

7.3 Organisms to be Protected

-

7.4 User

-

7.5 Resistance

-

8.1 Methods Handling and Storing

-

8.2 Fire Guidance

-

8.3 Emergency Measures

-

8.4 Possib. of Rendering Subst. Harmless

-

8.5 Waste Management

-

8.6 Side-effects Detection

-

8.7 Substance Registered as Dangerous for Ground Water

-

8.8 Reactivity Towards Container Material

-

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 - Indirect Photodegradation with AOPWIN v.1.91, 2000
 - Henry's Law Constant with HENRYWIN v.3.10, 2000
 - Distribution of tetrahydrofurfuryl alcohol based on Fugacity model (Levell III) with EPIWIN
 - Soil Adsorption Coefficient with PCKOCWIN v.1.66, 2000
 - Bioconcentration Factor with BCFWIN v.2.15, 2000

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- (35) TSCA Section 8(e):8EHQ-0995-13504 (1995b)
- (36) TSCA Section 8(e):8EHQ-0995-13505 (1995c)
- (37) TSCA Section 8(e):8EHQ-1091-1381A(1991)
- (38) TSCA Section 8(e):8EHQ-1092-8576S (1992c)
- (39) WHO/IPCS/ILO. (2004). International Chemical Safety Cards (ICSC: 1159).

10. Summary and Evaluation

10.1 End Point Summary

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10.2 Hazard Summary

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10.3 Risk Assessment

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