Robust Summaries of Reliable Studies and QSAR Model Data for Dimethyl Isophthalate (DMIP)

201-16425B

Appendix A

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2.1 MELTING POINT

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; MPBPWIN Program, Version 1.41, and PHYSPROP file (as periodically updated from Syracuse Research Corporation database); PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC). 1

2.2 BOILING POINT

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; MPBPWIN Program, Version 1.41, and PHYSPROP file (as periodically updated from Syracuse Research Corporation database); PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC). 3

2.4 VAPOR PRESSURE

Daubert, T.E. and Danner, R.P. (eds). 1993. Physical and Thermodynamic Properties of Pure Chemicals: Data compilation. Design Institute for Physical Property Data, American Institute of Chemical Engineers. Taylor & Francis. Washington, D.C 4

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; MPBPWIN Program, Version 1.41; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC). 5

2.5 PARTITION COEFFICIENT

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; KOWWIN Program, Version 1.67; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC). 6

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2.6 WATER SOLUBILITY

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; WSKOWWIN Program, Version 1.41; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC)

and

Chemicals Inspection and Testing Institute. 1992. Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan; Japan Chemical Industry Ecology - Toxicology and Information Center. ISBN 4-89074-101-1. QH545.b56.....7

3.1.1 PHOTODEGRADATION

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; AOPWIN Program, Version 1.91; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).....8

3.1.2 STABILITY IN WATER

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; HYDROWIN Program, Version 1.67; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).....9

3.3.2 TRANSPORTATION BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY MODEL)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC)..10-16

3.5 BIODEGRADATION

Japan Chemical Industry Ecology - Toxicology and Information Center. 1992. Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan. ISBN 4-89074-101-1. QH545.B56.....17

Gu, J.D., Li, J. and Wang, Y. 2005. Biochemical pathway and degradation of phthalate ester isomers by bacteria. Water Sci. Technol. 52(8):241-248.....18

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Kurane, R., Suzuki, T. and Takahara, Y. 1977. Isolation of microorganisms growing on phthalate esters by *Pseudomonas acidovorans* 256-1. Agri. Biol. Chem. 41(11):2119-2123.....21

Aleshchenkova, Z.; Samsonova, A.; Semochkina, N.; Baikova, S.; Tolstolutskaya, L. and Begel'man, M. 1997. Utilization of isophthalic acid esters by rhodococci. Microbiology. 66(5):616-620. [English translation].....22

Kurane, R., Suzuki, T., and Fukuoka, S. 1984. Purification and some properties of a phthalate ester-hydrolyzing enzyme from *Nocardia erythropolis*. Appl. Microbiol. Biotechnol. 20:378-383.....24

4.1 ACUTE/PROLONGED TOXICITY TO FISH

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; ECOSAR Version 0.99h; PC-Computer software developed by ECOSAR Program, Risk Assessment Division (7403), Washington, D.C. 26

4.2 TOXICITY TO AQUATIC INVERTEBRATES

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; ECOSAR Version 0.99h; PC-Computer software developed by ECOSAR Program, Risk Assessment Division (7403), Washington, D.C. 27

4.3 TOXICITY TO AQUATIC PLANTS (ALGAE)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; ECOSAR Version 0.99h; PC-Computer software developed by ECOSAR Program, Risk Assessment Division (7403), Washington, D.C. 28

5.10 ADDITIONAL STUDIES

Takahashi, T. and Tanaka, A. 1989. Biochemical studies on phthalic esters V: comparative studies on in vitro hydrolysis of di-*n*-butyl phthalate isomers in rats. Arch. Toxicol. 63(1):72-74.....29

2.1 MELTING POINT

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	EPIWIN (v 3.12) MPBPWIN Program (v 1.41) – Estimated value was determined to be the mean of the Adapted Joback and Gold & Ogle Methods.
GLP:	Not applicable
Year:	2006
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Melting Point:	Estimated (mean) = -22.74°C Experimental database structure match = 67.5°C (SRC Database)
Decomposition:	Not applicable
Sublimation:	Not applicable
Remarks:	The model-predicted value is not comparable to the experimental database value cited by the model's PHYSPROP file. This model-predicted value is not considered to be plausible since DMIP is a solid under ambient conditions. The experimental database value (instead of the modeled value) was used in subsequent EPI Suite™ subroutines, which were run in batch mode.

Conclusions

The endpoint has been adequately characterized (Vertellus Performance Materials Inc.).

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; model data.

Reference(s)	U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; MPBPWIN Program, Version 1.41, and PHYSPROP file (as periodically updated from Syracuse Research Corporation database); PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).
Other	
Last Changed:	November 2, 2006
Remark:	Key study

2.2 BOILING POINT

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	EPIWIN (v 3.12) MPBPWIN Program (v 1.41) – Estimated value was obtained using the adapted Stein and Brown method.
GLP:	Not applicable
Year:	2006
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Boiling Point:	Estimated = 248.83°C Experimental database structure match = 282°C
Pressure:	760
Pressure Unit:	mm Hg
Decomposition:	Not applicable
Remarks:	The experimental database value (instead of the modeled value) was used in subsequent EPI Suite™ subroutines, which were run in batch mode.

Conclusions

The endpoint has been adequately characterized (Vertellus Performance Materials Inc.).

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; model data.

Reference(s)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; MPBPWIN Program, Version 1.41, and PHYSPROP file (as periodically updated from Syracuse Research Corporation database); PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Other

Last Changed:	November 2, 2006
Remark:	Key study

2.4(1) VAPOR PRESSURE

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	Not stated
GLP:	Not stated
Year:	Not stated
Remarks:	Estimated value

Results

Vapor Pressure:	9.63×10^{-3} mm Hg
Temperature:	Not stated
Decomposition:	Not stated
Remarks:	None

Conclusions This literature value confirms the EPIWIN model estimate.

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; estimated data.

Reference(s) Daubert, T.E. and Danner, R.P. (eds). 1993. Physical and Thermodynamic Properties of Pure Chemicals: Data compilation. Design Institute for Physical Property Data, American Institute of Chemical Engineers. Taylor & Francis. Washington, D.C.

Other

Last Changed:	November 2, 2006
Remark:	Key study

2.4(2) VAPOR PRESSURE

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	EPIWIN (v 3.12) MPBPWIN Program (v 1.41) – Estimated value was obtained using the Modified Grain method.
GLP:	Not applicable
Year:	2006
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Vapor Pressure:	2.01×10^{-3} mm Hg
Temperature:	25°C
Decomposition:	Not applicable
Remarks:	None

Conclusions The endpoint has been adequately characterized (Vertellus Performance Materials Inc.).

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; model data.

Reference(s) U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; MPBPWIN Program, Version 1.41; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Other

Last Changed: October 12, 2006

2.5 PARTITION COEFFICIENT

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method:	EPIWIN (v 3.12), KOWWIN Program (v 1.67)
GLP:	Not applicable
Year:	2006
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Log K_{ow}:	1.66
Temperature:	25°C
Remarks:	None

Conclusions

The endpoint has been adequately characterized (Vertellus Performance Materials Inc.).

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; model data.

Reference(s)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; KOWWIN Program, Version 1.67; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Other

Last Changed:	November 2, 2006
Remark:	Key study

2.6 WATER SOLUBILITY

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	EPIWIN (v 3.12), WSKOWWIN Program (v 1.41)
GLP:	Not applicable
Year:	2006
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Solubility:	Estimated = 1778 mg/L Experimental database structure match = 290 mg/L (Chem. Inspect. Test Institute, 1992)
Temperature:	25°C
pH value and concentration:	Not applicable
pKa value at 25°C:	Not applicable
Remarks:	None

Conclusions The endpoint has been adequately characterized (Vertellus Performance Materials Inc.).

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; model data.

Reference(s)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; WSKOWWIN Program, Version 1.41; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

and

Chemicals Inspection and Testing Institute. 1992. Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan; Japan Chemical Industry Ecology - Toxicology and Information Center. ISBN 4-89074-101-1. QH545.b56.

Other

Last Changed:	November 2, 2006
Remark:	Key study

3.1.1 PHOTODEGRADATION

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/guideline followed:	EPIWIN (v 3.12), AOPWIN Program (v 1.91)
Type:	Not applicable
GLP:	Not applicable
Year:	2006
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Concentration of substance:	Not applicable
Temperature °C:	Not Stated
Direct photolysis:	Not applicable
Indirect photolysis:	Not applicable
Breakdown products:	Not applicable
Remarks:	Overall OH Rate Constant (k_{phot}) = 0.6365×10^{-12} cm^3/molecule·sec $t_{1/2}$ = 16.805 days (12-hour day; 1.5×10^6 OH/cm^3)

Conclusions

The endpoint has been adequately characterized (Vertellus Performance Materials Inc.).

Data Quality

Reliability (Klimisch):	2D
Remarks:	Reliable with restrictions; model data

Reference(s)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; AOPWIN Program, Version 1.91; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Other

Last changed:	November 2, 2006
Remark:	Key study

3.1.2 STABILITY IN WATER

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/guideline followed:	EPIWIN (v 3.12), HYDROWIN Program (v 1.67)
Type:	Not applicable
GLP:	Not applicable
Year:	2006
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Total K_b:	2.278×10^{-1} L/mol·sec
pH:	> 8
Temperature:	25°C
K_b Half-life at pH 8:	35.212 days
K_b Half-life at pH 7:	352.118 days
Remarks:	None

Conclusions

The endpoint has been adequately characterized (Vertellus Performance Materials Inc.).

Data Quality

Reliability (Klimisch):	2D
Remarks:	Reliable with restrictions; model data

Reference(s)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; HYDROWIN Program, Version 1.67; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Other

Last changed:	November 2, 2006
Remark:	Key study

3.3.2(1) TRANSPORTATION BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY MODEL)

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	EPIWIN (v 3.12) Level III Fugacity Model; adapted from Mackay's EQC Level III Fugacity Model
Media:	Water, air, soil and sediment (model run with 1000 kg/hr emissions each to air, water and soil)
GLP:	Not applicable
Year:	2006
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Remarks:	Following are the results from the model:

Conclusions

Mass Amounts:
- Air = 1.1%
- Water = 28.2%
- Soil = 70.6%
- Sediment < 0.1%

Remarks: The endpoint has been adequately characterized. (Vertellus Performance Materials Inc.).

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; model data.

Reference(s)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Other

Last changed:	November 2, 2006
Remark:	Key study

3.3.2(2) TRANSPORTATION BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY MODEL)

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	EPIWIN (v 3.12) Level III Fugacity Model; adapted from Mackay's EQC Level III Fugacity Model
Media:	Water, air, soil and sediment (model run with 1000 kg/hr emissions to air)
GLP:	Not applicable
Year:	2006
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Remarks:	Following are the results from the model:

Conclusions

Mass Amounts:
- Air = 2.9%
- Water = 14%
- Soil = 83%
- Sediment < 0.1%

Remarks: The endpoint has been adequately characterized. (Vertellus Performance Materials Inc.).

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; model data.

Reference(s)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Other

Last changed: October 12, 2006

3.3.2(3) TRANSPORTATION BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY MODEL)

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	EPIWIN (v 3.12) Level III Fugacity Model; adapted from Mackay's EQC Level III Fugacity Model
Media:	Water, air, soil and sediment (model run with 1000 kg/hr emissions to water)
GLP:	Not applicable
Year:	2006
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Remarks:	Following are the results from the model:

Conclusions

Mass Amounts:
- Air < 0.01%
- Water = 99.7%
- Soil < 0.1%
- Sediment = 0.3%

Remarks: The endpoint has been adequately characterized. (Vertellus Performance Materials Inc.).

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; model data.

Reference(s)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Other

Last changed:	October 12, 2006

3.3.2(4) TRANSPORTATION BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY MODEL)

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	EPIWIN (v 3.12) Level III Fugacity Model; adapted from Mackay's EQC Level III Fugacity Model
Media:	Water, air, soil and sediment (model run with 1000 kg/hr emissions to soil)
GLP:	Not applicable
Year:	2006
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Remarks:	Following are the results from the model:

Conclusions

Mass Amounts:
- Air < 0.1%
- Water = 10.3%
- Soil = 89.6%
- Sediment < 0.1%

Remarks: The endpoint has been adequately characterized. (Vertellus Performance Materials Inc.).

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; model data.

Reference(s)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Other

Last changed:	October 12, 2006

3.3.2(5) TRANSPORTATION BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY MODEL)

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	EPIWIN (v 3.12) Level III Fugacity Model; adapted from Mackay's EQC Level III Fugacity Model
Media:	Water, air, soil and sediment (model run with 1000 kg/hr emissions each to air and water)
GLP:	Not applicable
Year:	2006
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Remarks:	Following are the results from the model:

Conclusions

Mass Amounts:
- Air = 1.9%
- Water = 43.7%
- Soil = 54.3%
- Sediment = 0.1%

Remarks: The endpoint has been adequately characterized. (Vertellus Performance Materials Inc.).

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; model data.

Reference(s)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Other

Last changed:	October 12, 2006

3.3.2(6) TRANSPORTATION BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY MODEL)

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	EPIWIN (v 3.12) Level III Fugacity Model; adapted from Mackay's EQC Level III Fugacity Model
Media:	Water, air, soil and sediment (model run with 1000 kg/hr emissions each to air and soil)
GLP:	Not applicable
Year:	2006
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Remarks:	Following are the results from the model:

Conclusions

Mass Amounts:
- Air = 1.3%
- Water = 11.9%
- Soil = 86.8%
- Sediment < 0.1%

Remarks: The endpoint has been adequately characterized. (Vertellus Performance Materials Inc.).

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; model data.

Reference(s)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Other

Last changed:	October 12, 2006

3.3.2(7) TRANSPORTATION BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY MODEL)

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	EPIWIN (v 3.12) Level III Fugacity Model; adapted from Mackay's EQC Level III Fugacity Model
Media:	Water, air, soil and sediment (model run with 1000 kg/hr emissions each to water and soil)
GLP:	Not applicable
Year:	2006
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Remarks:	Following are the results from the model:

Conclusions

Mass Amounts:
- Air < 0.1%
- Water = 35.9%
- Soil = 63.9%
- Sediment < 0.1%

Remarks: The endpoint has been adequately characterized. (Vertellus Performance Materials Inc.).

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; model data.

Reference(s)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Other

Last changed:	October 12, 2006

3.5(1) BIODEGRADATION

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	OECD 301-C
Test Type:	MITI method
GLP:	Not stated
Year:	Not stated
Contact Time:	14 days
Inoculum:	Activated sludge (30 ppm)
Analytical Monitoring:	Direct analysis: HPLC and TOC; Indirect analysis: BOD
Remarks:	Test concentration was 100 ppm.

Results

Degradation:	Test substance was determined to be readily biodegradable.
Results:	Biodegradability based on indirect analysis was 99% after two weeks. Direct analysis by HPLC and TOC measurement confirmed biodegradability over the two week study period to be 100% and 96%, respectively.
Kinetic:	Not stated.
Breakdown Products:	Not stated.

Conclusions

Biodegradability as a measure of BOD, TOC and test substance concentration has been adequately characterized (Vertellus Performance Materials Inc.).

Data Quality

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

Reference(s)

Japan Chemical Industry Ecology - Toxicology and Information Center. 1992. Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan. ISBN 4-89074-101-1. QH545.B56.

Other

Last Changed:	November 2, 2006
Remark:	Key study

3.5(2) BIODEGRADATION

Test Substance

Identity:	Dimethyl isophthalate (DMIP; DMI; CAS RN 1459-93-4)
Purity:	Not stated

Method

Method/Guideline followed:	Not stated
Test Type:	Bacterial degradation
GLP:	Not stated
Year:	2005
Contact Time:	12 days
Inoculum:	Mangrove sediments from the Mai Po Nature Reserve of Hong Kong, China.
Analytical Monitoring:	High-performance liquid chromatography (HPLC) equipped with a diode array UV-visible detector set at 254 nm (primary wavelength), 236 nm (secondary wavelength) and 280 nm (background reference).
Remarks:	The initial culture was established by adding 1.0 g of the mangrove sediment to 100 mL of mineral salt medium in a 250-mL flask with DMIP (100 mg/L) as the sole energy and carbon source. The initial adjusted pH of the culture medium was 7.0±0.1. Following purification and streaking on agar plates, isolates were gram stained and primary bacteria identification was performed using the API 20NE Multitest Kit. Each of three bacteria isolated from the initial culture were tested for their abilities to grow on minimal agar plates and in liquid culture with DMIP, monomethyl isophthalate (MMIP) and isophthalate (IPA). Based on the results of this preliminary test, degradation of DMIP was investigated using two Gram-negative, rod-shaped bacteria. These isolates were identified as *Klebsiella oxytoca* Sc (96.1% similarity by API 20E) and *Methylobacterium mesophilicum* Sr (93.7% similarity by API 20E). Chemical concentration in the culture sample was determined by using HPLC (see analytical details above). During degradation, microbial biomass was determined by optical density (OD) measurements at 600 nm spectrophotometrically using an UV 1201.

Results

Degradation: 100% degradation in approximately 36 hours

Results: DMIP could not be degraded by complete mineralization by either of the two isolates alone. While *K. oxytoca* Sc was able to completely transform DMIP (108 mg/L) to MMIP within approximately 36 hours (Figure 1), MMIP accumulated in the culture medium over this period and did not decrease over the extended incubation period (*i.e.* through five days). *M. mesophilicum* Sr was able to degrade the intermediate MMIP to IPA within approximately 8 days (Figure 2). Both species demonstrated metabolism of IPA.

Kinetic:

Figure 1: Degradation of DMIP by *Klebsiella oxytoca* Sc isolated from mangrove sediment.

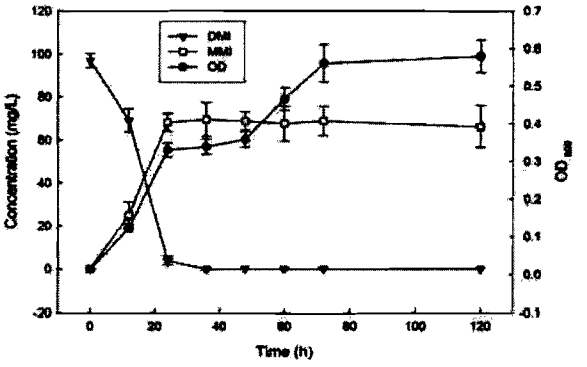
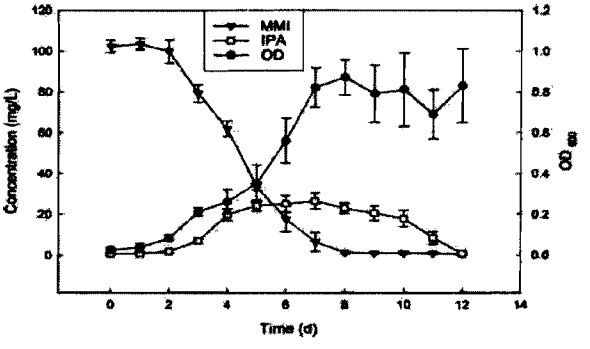


Figure 2: Degradation of MMIP by *Methylobacterium mesophilicum* Sr isolated from mangrove sediment.



Breakdown Products: Monomethyl isophthalate (MMIP); isophthalate (IPA)

Remarks: None

Conclusions	Degradation of DMIP was demonstrated with a mixed bacterial culture from mangrove sediment; however, complete degradation required the biochemical cooperation between selective bacterial species. The initial reactions involved hydrolysis of the ester bonds of DMIP and MMIP. Biodegradability has been adequately characterized (Vertellus Performance Materials Inc.).
Data Quality	
Reliability:	2A
Remarks:	Reliable with restriction; acceptable, well-documented publication which meets basic scientific principles.
Reference(s)	Gu, J.D., Li, J. and Wang, Y. 2005. Biochemical pathway and degradation of phthalate ester isomers by bacteria. Water Sci. Technol. 52(8):241-248.
Other	
Last Changed:	November 2, 2006

3.5(3) BIODEGRADATION

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not stated

Method

Method/Guideline followed:	Not stated
Test Type:	Bacterial degradation
GLP:	Not stated
Year:	1977
Contact Time:	40 days
Inoculum:	*Pseudomonas acidovorans* 256-1 (Isolated from soil and wastewater)
Analytical Monitoring:	Gas chromatography
Remarks:	6000 ppm of DMIP was incubated (shaken at 30°C) with *Pseudomonas acidovorans* 256-1 for 40-days. The time required for the degradation of 3000 ppm was measured.

Results

Degradation:	No degradation was noted.
Results:	No degradation was noted.
Kinetic:	Not stated.
Breakdown Products:	Not stated.

Conclusions

This study design is limited and does not adequately characterize this endpoint (Vertellus Performance Materials Inc.).

Data Quality

Reliability:	3C
Remarks:	Not reliable; does not meet important criteria for today's standard methods.

Reference(s)

Kurane, R., Suzuki, T. and Takahara, Y. 1977. Isolation of microorganisms growing on phthalate esters by *Pseudomonas acidovorans* 256-1. Agri. Biol. Chem. 41(11):2119-2123.

Other

Last Changed:	November 2, 2006

3.5(4) BIODEGRADATION

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not stated

Method

Method/Guideline followed:	Not stated
Test Type:	Bacterial degradation
GLP:	Not stated
Year:	1997
Contact Time:	28 days
Inoculum:	*Rhodococcus erytropolis* 5D extract, isolated from soil contaminated with phthalic esters in natural conditions; isolated by accumulative culture method. A *R. erythopolis* 100 B and *R. rubber* 1B extract was also isolated from the active sludge of a chemical production waste treatment plant.
Analytical Monitoring:	Quantitative analysis of DMIP was performed using a Chrom-5 gas chromatography method. Metabolic by-products of DMIP were extracted three times and identified by thin-layer chromatography on Silufol UV-254 plates in hexane:ethyl acetate:formylic [formic] acid (12:7:0.5). UV-spectra of metabolites in the ethyl alcohol were recorded on Specord M-40.
Remarks:	*The Rhodococcus erytropolis* 5D extract was isolated by an accumulative culture method and cultured in a mineral medium at pH 7.3. These cultures contained DMIP at a concentration of 0.1-0.5%, which served as the carbon source. These cultures were maintained in 250-mL Erlenmeyer flasks with 50 mL of mineral medium. After incubation for 168 hours at 29°C with continuous shaking (180 rpm), the number of living cells was determined. The isophthalic acides were extracted from the medium using diethyl ester and ethyl alcohol. The main degradation experiment was conducted at DMIP concentrations of 0.1% and 0.2% over 28 days at a constant temperature (25°C) and humidity (60% saturation).

Results

Degradation:	*R. rubber* 1B: 100% degradation of 0.1 and 0.2% DMIP in 168 hours. *R. erythropolis* 5D: 100% degradation of 0.1% DMIP in 96 hours and 0.2% DMIP in 168 hours.

Results:	See above.
Kinetic:	Not reported for DMIP
Breakdown Products:	Isophthalate, benzoic, n-hydroxy benzoic, protocatechik [protocatechic] acids as well as protocatechol, and monomethyl isophthalate.
Remarks:	None

Conclusions

Biodegradability has been adequately characterized (Vertellus Performance Materials Inc.).

Data Quality

Reliability:	3B
Remarks:	Not reliable; documentation insufficient for assessment.

Reference(s)

Aleshchenkova, Z.; Samsonova, A.; Semochkina, N.; Baikova, S.; Tolstolutskaya, L. and Begel'man, M. 1997. Utilization of isophthalic acid esters by rhodococci. Microbiology. 66(5):616-620. [English translation]

Other

Last Changed:	November 2, 2006

3.5(5) BIODEGRADATION

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	Not stated
Test Type:	Bacterial degradation
GLP:	Not stated
Year:	1984
Contact Time:	18 hours
Inoculum:	Phthalate-ester hydrolyzing enzyme purified from *Nocardia erythropolis* S-1 (also classified as *Rhodococcus erythropolis*)
Analytical Monitoring:	Gas chromatography-mass spectrometry (GC-MS) with ionization energy
Remarks:	In addition to investigating the purification, homogeneity, molecular weight, and effects of pH, temperature, cations and reagents on the activity, this study examined the substrate specificity of the phthalate-ester hydrolyzing enzyme extracted from *Nocardia erythropolis* S-1. The positional specificity of the hydrolysis reaction was also investigated. The enzyme reaction mixture (5.0 mL) was made up of the substrate (DMIP, 10,000 ppm) in Tris-HCl buffer (μ=0.05, pH 8) with 0.5% $CaCl_2$ solution and enzyme solution. The reaction mixture was incubated on a reciprocal shaker at 30°C for 18 h. The enzyme reaction mixture was extracted with *n*-hexane followed by diethyl ether (pH 2). Then, the diethyl ether extract was methylated with diazomethane, which yielded dimethyl phthalate (DMP). This reaction/extraction product was quantified on a glass column, using anthrone as an internal standard. Structure was confirmed by GC-MS with ionization energy.

Results

Degradation:	Relative enzyme activity: 4.3%
Results:	The phthalate-ester hydrolyzing enzyme hydrolyzed most of the phthalate esters tested, regardless of side chain type. The enzyme readily hydrolyzed dimethyl isophthalate.
Kinetic:	Not reported.

Breakdown Products:	Not reported.
Conclusions	The phthalate-ester hydrolyzing enzyme from *N. erythropolis* was concluded to be a lipase of low substrate specificity. Distribution of the enzyme was observed to be intra- and extracellular, suggesting that *N. erythropolis* secretes the enzyme that hydrolyzes phthalate esters without accumulation of phthalate monoester. However, it remains unclear as to whether the enzyme purified from culture broth in this study is comparable to its intracellular counterpart.
Data Quality	
Reliability:	3C
Remarks:	Not reliable; does not meet important criteria for today's standard methods.
Reference(s)	Kurane, R., Suzuki, T., and Fukuoka, S. 1984. Purification and some properties of a phthalate ester-hydrolyzing enzyme from *Nocardia erythropolis*. Appl. Microbiol. Biotechnol. 20:378-383.
Other	
Last Changed:	November 2, 2006

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	EPIWIN (v 3.12) ECOSAR Program (v 0.99h)
Type:	Not applicable
GLP:	Not applicable
Year:	2006
Species/Strain/Supplier:	Fathead minnow (*Pimephales promelas*)
Analytical monitoring:	Not applicable
Exposure period:	96-hour
Statistical methods:	Not applicable
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Nominal concentrations (mg/l):	Not applicable
Measured concentrations (mg/l):	Not applicable
Unit:	mg/l
Element value:	96-hour LC_{50} = 44.681 mg/l
Statistical results:	Not applicable
Remarks:	None

Conclusions

Remarks:	The endpoint has been adequately characterized (Vertellus Performance Materials Inc.).

Data Quality

Reliability (Klimisch):	2D
Remarks:	Reliable with restrictions; model data.

Reference(s)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; ECOSAR Version 0.99h; PC-Computer software developed by ECOSAR Program, Risk Assessment Division (7403), Washington, D.C.

Other

Last changed:	October 30, 2006
Remark:	Key study

4.2 TOXICITY TO AQUATIC INVERTEBRATES

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	EPIWIN (v 3.12) ECOSAR Program (v 0.99h)
Type:	Not applicable
GLP:	Not applicable
Year:	2003
Species/Strain/Supplier:	Daphnid (*Daphnia magna*)
Analytical monitoring:	Not applicable
Exposure period:	48-hour
Statistical methods:	Not applicable
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Nominal concentrations (mg/l):	Not applicable
Measured concentrations (mg/l):	Not applicable
Unit:	mg/l
Element value:	48-hour LC_{50} = 314.502 mg/l
Statistical results:	Not applicable
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized (Vertellus Performance Materials Inc.).

Data Quality

Reliability (Klimisch):	2D
Remarks:	Reliable with restrictions; model data.

Reference(s)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; ECOSAR Version 0.99h; PC-Computer software developed by ECOSAR Program, Risk Assessment Division (7403), Washington, D.C.

Other

Last changed:	October 30, 2006
Remark:	Key study

4.3 TOXICITY TO AQUATIC PLANTS (ALGAE)

Test Substance

Identity:	Dimethyl isophthalate (DMIP; CAS RN 1459-93-4)
Purity:	Not applicable

Method

Method/Guideline followed:	EPIWIN (v 3.12) ECOSAR Program (v 0.99h)
Type:	Not applicable
GLP:	Not applicable
Year:	2003
Species/Strain/Supplier:	Green Algae (*Selenastrum capricornutum)*
Analytical monitoring:	Not applicable
Exposure period:	96-hour
Statistical methods:	Not applicable
Remarks:	The EPIWIN model was not run with any physico-chemical property input values.

Results

Nominal concentrations (mg/l):	Not applicable
Measured concentrations (mg/l):	Not applicable
Unit:	mg/l
Element value:	96-hour EC_{50} = 3.513 mg/l
Statistical results:	Not applicable
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized (Vertellus Performance Materials Inc.).

Data Quality

Reliability (Klimisch):	2D
Remarks:	Reliable with restrictions; model data.

Reference(s)

U.S. EPA (Environmental Protection Agency). 2000. EPI Suite™, Version 3.12; ECOSAR Version 0.99h; PC-Computer software developed by ECOSAR Program, Risk Assessment Division (7403), Washington, D.C.

Other

Last changed:	October 30, 2006
Remark:	Key study

5.10 ADDITIONAL STUDIES

Test Substance

Identity:	Dibutyl isophthalate (DBIP), Dibutyl terephthalate (DBTP) and Dibutyl phthalate (DBP)
Purity:	Not stated

Method

Method/guideline followed:	Not stated
Type:	*In vitro* incubation
GLP:	Not stated
Year:	1989
Species/Strain:	Wistar rat tissue preparations
Metabolic activation:	No
Concentration tested:	0.04 mmol/reaction
Statistical Methods:	Not stated
Remarks:	One of the test substances, DBIP, is a structural analog of DMIP. The study measured the *in vitro* hydrolysis of phthalate ester isomers by rat tissue preparations after a 60 minute incubation period. Tissue preparation: Male Wistar rats were sacrificed by decapitation after overnight fasting and the liver, pancreas, small intestines and kidneys were removed immediately. Serum was also obtained. Subcellular fractionations of the liver and other tissues were prepared according to cited literature. The tissue preparations utilized are as follows: liver (homogenate, mitochondria, microsome and supernatant), pancreas, small intestine, kidney and blood serum. Test conditions: The reaction mixture consisted of a phthalic ester substrate (0.4 ml of 0.1 M), phosphate buffer (0.5 ml of 0.2 M) and enzyme preparation (0.5 ml) in a total volume of 2 ml. The reactions were incubated for 60 minutes at 38°C. At the end of the incubation period, the incubation mixture was extracted with ethyl acetate, concentrated and methylated with diazomethane. The methyl esters of the metabolites formed were analyzed by gas chromatography (Shimadzu GC-7A with dual hydrogen flame ionization detectors).

Results

Metabolites Formed: DBIP → IPA (Isophthalic acid) and MBIP (Monobutyl isophthalate)
DBTP → TPA (Terephthalic acid) and MBTP (Monobutyl terephthalate)
DBP → MBP (Monobutyl phthalate)

Remarks: Of the organs examined, the pancreas demonstrated the maximal activity for de-esterification. Hydrolysis of phthalic acid isomers also occurred at high rates in hepatic tissue, especially the liver microsomes. The renal hydrolysis of DBIP to IPA was more than double the renal hydrolysis of DBTP to TPA. DBIP and DBTP were hydrolyzed to their respective acids, IPA and TPA, by rat tissue enzymes; however, the acid formation was slower than the mono-ester formation.

Enzyme Sources	Products Formed* (nmoles/mg·protein/min)				
Substrate:	DBIP		DBTP		DBP
Metabolite:	IPA	MBIP	TPA	MBTP	MBP
Liver					
Homogenate	3.1 ± 0.7	26.5 ± 4.0	1.8 ± 0.2	33.3 ± 6.0	14.5 ± 2.1
Mitochondria	1.5 ± 0.2	13.4 ± 0.7	0.6 ± 0.1	11.1 ± 1.2	9.4 ± 0.8
Microsome	13.5 ± 1.6	103.1 ± 15.1	7.5 ± 1.2	129.2 ± 14.8	58.9 ± 7.8
Supernatant	0.4 ± 0.1	16.0 ± 1.5	ND	ND	2.0 ± 0.2
Pancreas	0.5 ± 0.1	73.5 ± 8.4	2.1 ± 0.3	54.7 ± 4.7	56.2 ± 6.6
Small Intestine	0.1 ± 0.0	16.3 ± 2.3	4.2 ± 0.8	11.1 ± 2.6	7.5 ± 1.9
Kidney	3.6 ± 0.4	23.4 ± 2.0	1.5 ± 0.2	44.4 ± 2.5	13.0 ± 1.4
Blood	0.1 ± 0.0	6.8 ± 0.5	0.1 ± 0.0	12.6 ± 1.6	3.3 ± 0.4

* Values are the mean ± standard deviation of at least three runs.
DBIP = Dibutyl isophthalate; DBTP = Dibutyl terephalate
IPA = Isophthalic acid; MBIP = Monobutyl isophthalate
TPA = Terephthalic acid; MBTP = Monobutyl terephthalate
DBP = Dibutyl phthalate; MBP = Monobutyl phthalate
ND = Not determined.

Conclusions

Remarks: DBIP and DBTP were hydrolyzed to their corresponding acids, IPA and TPA, by rat tissue enzymes. DMIP is anticipated to follow the same metabolic pathways. The endpoint has been adequately characterized (Vertellus Performance Materials Inc.).

Data Quality

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

Reference(s)

Takahashi, T. and Tanaka, A. 1989. Biochemical studies on phthalic esters V: comparative studies on in vitro hydrolysis of di-*n*-butyl phthalate isomers in rats. Arch. Toxicol. 63(1):72-74.

Other

Last Changed:	November 2, 2006
Remark:	Key study

Appendix B

OECD SIDS Submissions (SIAP and SIAR Dossier) and IUCLID Datasets for Dimethyl Terephthalate, Isophthalic Acid and Terephthalic Acid

Index of OECD SIDS Submissions (SIAP and SIAR Dossiers) and IUCLID Datasets for Dimethyl Terephthalate, Isophthalic Acid and Terephthalic Acid

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OECD SIDS Submissions (SIAP and SIAR Dossier) for Dimethyl terephthalate (CAS RN 120-61-6), Submitted November 7, 2000. 2

IUCLID Dataset for Dimethyl terephthalate (CAS RN 120-61-6), Submitted February 18, 2000. 93

2. ISOPHTHALIC ACID (CAS RN 121-91-5) 156

OECD SIDS Submissions (SIAP and SIAR Dossier) for Isophthalic acid (CAS RN 121-91-5), Submitted February 1, 2002. 157

IUCLID Dataset for Isophthalic acid (CAS RN 121-91-5), Submitted February 18, 2000. 267

3. TEREPHTHALIC ACID (CAS RN 100-21-0) 294

OECD SIDS Submissions (SIAP and SIAR Dossier) for Terephthalic acid (CAS RN 100-21-0), Submitted June, 2001. 295

IUCLID Dataset for Terephthalic acid (CAS RN 100-21-0), Submitted February 22, 2000. 378

SECTION 1.

DIMETHYL TEREPHTHALATE (CAS RN 120-61-6)

OECD SIDS SUBMISSIONS (SIAP AND SIAR DOSSIER) FOR

DIMETHYL TEREPHTHALATE (CAS RN 120-61-6)

FOREWORD INTRODUCTION

Dimethyl terephthalate

CAS N°: 120-61-6

SIDS Initial Assessment Report

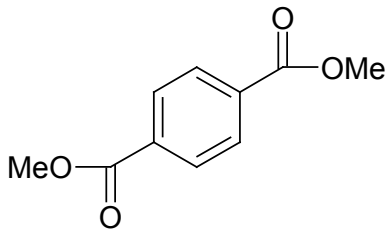
For

SIAM 11

United States, January 23-26, 2001

1. Chemical Name:	Dimethyl terephthalate
2. CAS Number:	120-61-6
3. Sponsor Country:	United States/IT
	National SIDS Contact Point in Sponsor Country: Oscar Hernandez Director, Risk Assessment Division Office of Pollution Prevention and Toxics US EPA Washington, DC 20460
4. Shared Partnership with:	
5. Roles/Responsibilities of the Partners:	
• Name of industry sponsor /consortium	
• Process used	
6. Sponsorship History	SIAM 3—Removed from Agenda for further work.
• How was the chemical or category brought into the OECD HPV Chemicals Programme ?	
7. Review Process Prior to the SIAM:	
8. Quality check process:	
9. Date of Submission:	November 7, 2000
10. Date of last Update:	
11. Comments:	

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	120-61-6
Chemical Name	Dimethyl Terephthalate
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Category/Analogue Rationale

Data for dimethylterephthalate (DMT) is available for all SIDS health endpoints. However, for reproductive and developmental toxicity, the available data on DMT is not considered sufficient to support a conclusion that these endpoints have been completed. As a result, additional data from terephthalic acid (TPA) is being presented to support the conclusion that the reproductive and developmental toxicity endpoints have been completed. The use of TPA data for health endpoints is acceptable due to the principle that DMT metabolizes to form TPA.

Human Health

Results from acute toxicity studies via the oral, dermal and inhalation routes indicate that DMT is of a low order of toxicity. Oral acute toxicity studies in rats reported LD50s of 4,390 to >6,590 mg/kg. Inhalation and dermal LC and LD50s in rats and guinea pigs were >6 mg/L and >5,000 mg/kg, respectively. In several animal studies, DMT is indicated to be slightly irritating to both the skin and eyes. Available data indicate that DMT is not considered to be sensitizing in guinea pigs.

Numerous repeat dose studies have been conducted via oral (gavage and dietary) and inhalation routes of exposure. Studies range in duration from 2-13 weeks via the oral route and up to six months for inhalation administrations. Collectively, the data indicate that the primary target organ is the urinary tract due to DMTs metabolism to TPA and the formation of renal crystals or calculi and their sequelae on the soft tissues. In a 14-day feeding study in rats a NOEL based on decreased body weights was seen in males at 660 mg/kg/day (0.5% in diet) and in females exposed to 1277 mg/kg/day (1.0% in diet) (Chin et al, 1981). In the same study, a NOEL for induction of urinary calculi was 1320 mg/kg (males) and 1790 mg/kg females (1.5% in diet). In a 96-day feeding study in rats, a NOEL, based on decreased body weight gains, of 313 mg/kg/day (0.5% in diet) and a LOAEL of 636 mg/kg/day (1% in diet) was determined. However, in this study, there was no evidence of urinary calculi (Krasavage et al., 1973). Thus, the formation of urinary calculi and its secondary effect on soft tissues occurred at a minimum DMT exposure length of 14 days at a dietary concentration of 1.5% for males (1,890 mg/kg) and 2% in females (2,290 mg/kg). Based on urinary solubility of Ca-TPA, normal human urine would become saturated with Ca-TPA at a TPA concentration of approximately 8-16mM. Assuming an average volume of urine excreted by humans is 1.5 L/day and that DMT is metabolized entirely to TPA, then the amount of DMT that would have to be absorbed to produce 8mM minimum saturating concentration of TPA is 2,400 mg/kg/day. Inhalation repeat dose studies do not show the primary urinary effect observed in the oral studies, however, following 90-days of exposure via the inhalation route, a NOAEL of 16.5 mg/m^3 was determined for the following effects: mild and transient clinical effects-nose rubbing, preening, and blinking. In the same study, a LOAEC of 86.4 mg/m^3 was established.

Given the weight of evidence, DMT does not appear to be mutagenic or genotoxic in numerous *in vitro* (bacterial and mammalian systems) and several *in vivo* studies. In addition, DMT was not deemed to have carcinogenic effects in a two year feeding study in male and female rats and female mice, but equivocal evidence was noted in male mice.

In developmental toxicity studies, two on DMT and one on TPA, there is no evidence of developmental toxicity. In inhalation studies, the NOAEC for DMT was 1 mg/m^3 and for TPA it was 10 mg/m^3 (both were the highest dose tested). In a gavage study on DMT, a NOAEL of >1000 mg/kg was determined. In a 115-day oral feeding study to assess the reproductive toxicity potential of DMT, a NOEL of 636 mg/kg/day (1.0% in diet; highest dose tested) was determined for parental effects while the NOEL for offspring was 152 mg/kg/day based on reduced pup weights at weaning. This effect was likely due to exposure to DMT through lactation and having access to the mother's food and hence it is a primary toxicity of DMT. Since this study's methodology varies from the current OECD guidelines, data from the DMT metabolite TPA is used to support this endpoint. In a one-generation reproduction feeding study on TPA, postnatal growth weight and mortality effects were observed in pups. The NOAEL for maternal toxicity and for the F1 offspring was 0.5% (240 to 307 mg/kg), while the NOAEL for reproductive effects was >5.0% (2480-3018 mg/kg) TPA in the diet. The adverse effects observed in the offspring in this study appear to be the result of maternal toxicity and the formation of renal and bladder calculi found in the weanling animals.

Environment

The physical-chemical properties of DMT include a melting point of 141^{0}C, a vapor pressure of 0.01 mmHg at 25^o C, a water solubility of approximately 19 - 37mg/l, a partition coefficient of log Kow 2.25 and a flash point of 153 ^{0}C. Overall, DMT undergoes slow abiotic hydrolysis (half-life 321 days), has a photo-oxidation half-life of weeks, and stability in surface and ground water with half-lives of weeks. However, the potential for significant environmental releases are low and the material is classified as readily biodegradable (84%, MITI test).
This chemical is moderately toxic to fish (96h LC50 = 9.6 mg/L), daphnids (48h LC50 = 30.4 mg/L), and green algae (72h EC_{50} biomass = 27.6 mg/L; 72h EC_{50} growth rate >32.3 mg/L). However, it is not expected to bioaccumulate in fish and is not expected to biomagnify via food chains. Using an assessment factor of 100 and the fish toxicity value, a PNEC of 0.096 mg/L is derived.

Exposure

Dimethyl terephthalate is produced (2004 world nameplate capacity estimate 4,936,000 tonnes or 1.09E10 pounds) in closed systems and used primarily within its own manufacturing facilities as a building block in the synthesis of polyethylene terephthalate plastics. It is also used as an intermediate to manufacture dioctyl terephthalate. When transported, it is shipped in bulk containers. Human exposures are in general very minimal and limited. The main occupational exposure concern in processing is that of direct physical burns due to accidental dermal contact to DMT in its molten state. Consumer exposure is possible via residual levels of less than 1 ppm DMT in PET-polymers.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

No recommendation for further work.

FULL SIDS SUMMARY

STUDY (CAS NO 120-61-6)		SPECIES	PROTOCOL	RESULTS
PHYSICAL CHEMISTRY				
2.1	Melting Point or Decomposition Point			141° C
2.2	Boiling Point			280° C and 288° C
2.3	Vapor Pressure			100 mmHg at 208° C; 1.15 mmHg at 93° C; 0.01 mmHg at 25° C
2.4	Partition Coefficient (Log Pow)			2.25
2.5	Water Solubility			19 mg/L (20°C) 37.2 mg/L (25° C)
2.6	Flashpoint		Cleveland, open cup	153° C
2.7	Flammability			NA
2.8	pH in water			NA
2.9	Other data: Explosive limits (Lower) Viscosity Surface Tension			 0.000033 mg/L NA NA
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Biodegradability		Chemical oxygen demand (aerobic)	COD = 1.70 g oxygen
			Japanese MITI test	Theoretical BOD = 84%
			River water and sea water tests	100% degradation in river water and up to 49% in sea water.
		Pseudomonas acidovorans	Incubation test	No degradation was noted.
		Rhodococcus	Incubation test	100% degradation
		Rhodococcus	Soil and wastewater inoculation tests	100 % degradation
		Bacillus sp.	Incubation test	DMT was its sole carbon source.
		Aspergillus niger	Incubation test	58% degradation after 144 hours
3.1.2	Sewage Treatment		Secondary waste water	IC_{50} = >5000 mg/L
3.1.3	Stability in air		Hydroxyl radical and ozone reactivity	$t_{1/2} \cong$ 3 days unreactive toward ozone.
			Photooxidation half-life	$t_{1/2}$ = 4.7 – 46.6 days.
	Stability in water		Alkoxyradical reactivity	Unreactive
			Hydrolytic half-life	321 days
			Half-life	Surface water $t_{1/2}$ = 1-4 Groundwater $t_{1/2}$ = 2-8 weeks
			Octanol water partition coefficient	LogP = 2.25
			Log sediment organic content/water partition coefficient	K_{oc} = 2.49
	Stability in soil		Half-life	1-4 weeks.
3.1.4	Identification of main mode of degradability in actual use	No specific studies available		
3.2	Bioaccumulation		Bioconcentration factor (Log)	BCF = 1.21
3.3	Photodegradation		Photooxidation half-life	4.7 – 46.6 days.

ECOTOXICOLOGICAL DATA				
4.1	Toxicity to fish			
4.1.1	Acute test	Fathead minnow	96 hr, static	LC_{50} = 9.6 mg/L
		Fathead minnow	96 hr, static	LC_{50} = 45 mg/L
		Fathead minnow	96 hr	LC_{50} = 14.2 mg/L
4.1.2	Results of long-term tests (e.g. prolonged toxicity) early life state	No studies available		
4.2	Toxicity to Daphnids			
4.2.1	Acute tests	*Daphnia*	96 hr	LC_{50} = >100 mg/L
		Daphnia	48 hr	EC_{50} = >30 mg/L
		Daphnia	48 hr	LC_{50} = 30.4 mg/L
4.2.2	Results of longer-term tests (e.g. reproduction)	No studies available		
4.3	Toxicity to algae	*Scenedesmus* *Subspicatus*	72 hr	Biomass EC_{50}: 27.6 mg/L EC_{10}: 14.3 mg/L NOEC: 10.8 mg/L Growth Rate EC_{50}: >32.3 mg/L EC_{10}: 20.1 mg/L NOEC: 10.8 mg/L
4.4	Toxicity to other aquatic organisms	Flatworm	96 hr, static	LC_{50} = >100 mg/L
		Snail	96 hr, static	LC_{50} = >30 mg/L
		Snail	96 hr, static	LC_{50} = >100 mg/L
		Sideswimmer	96 hr, static	LC_{50} = >30 mg/L
4.5	Toxicity to Bacteria	No studies available		
4.6	Toxicity to terrestrial organisms	No studies available		
4.6.1	Toxicity to Soil-dwelling organisms	No studies available		
4.6.2	Toxicity to Plants		Germination Effects	NOAEC = 10 mg/L (Rye grass) NOAEC = 30 mg/L (Radish, Lettuce)
				NOAEC = 10 mg/L (Rye grass, Radish) NOAEC = 1 mg/L (Lettuce)
			Seedling Effects	33 mg/L (Corn) 33 mg/L (Marigold) 33 mg/L (Lettuce) 10 mg/L (Radish)
				1000 mg/L (Radish, Marigold, Lettuce) 100 mg/L (Corn)
4.6.3	Toxicity to insects	No studies available		
4.6.4	Toxicity to Birds	No studies available		
4.7	Biological effects monitoring (including biomagnification)		Bioconcentration factor (Log)	BCF = 1.21
4.8	Biotransformation and Kinetics in Environmental Species	No studies available		
TOXICOLOGICAL DATA				
5.1	Acute Toxicity			
5.1.1	Acute Oral	Rat	20% solution in corn oil	LD_{50} > 6,590 mg/Kg
		Rat		LD_{50} = 4,390 mg/Kg
5.1.2	Acute Inhalation	Rat	Aerosol	LC_{50} = >6 mg/L
5.1.3	Acute Dermal	Guinea Pig	Unknown	LD_{50} = >5,000 mg/Kg
5.1.4	Acute other route	No studies available		
5.2	Corrosive/irritation	Guinea Pig	Inhalation via gauze	Slight redness, no edema
		Guinea Pig	Inhalation via gauze	Erythema and slight to moderate edema
		Mouse	Dermal, tails	A transient slight and behavioral changes
		Rabbit	Dermal, shaved skin	A slight irritation and pigmentation
5.3	Skin sensitization	Guinea Pig	Dermal, rump and	No sensitization response

			shoulders	
		Guinea Pig	Dermal, rump and footpads	No sensitization response
		Guinea Pig	Dermal	Slight irritation, no sensitization response
5.4	Repeat Dose	Rat	10 days, oral gavage	No NOEL was determined.
		Rat	14 days, oral diet	NOEL = 0.5% (male rats) NOEL = 1.0% (female rats)
		Rat	16 days, oral diet	A NOEL was not determined.
		Rat	28 day, oral diet	No hematological or histopathological abnormalities.
		Rat	>34 days, oral	NOEL = 500 mg/kg.
		Rat	13 weeks, oral	A NOEL was not determined.
		Rat and Mouse	13 weeks, oral diet	NOAEL = 5000 ppm (rats) NOAEL = 20000 ppm (mice)
		Rat	96 days, oral diet	NOEL = 313 mg/kg
		Rat	5 months, inhalation	30% mortality, rhinitis, depilation, dystrophic changes in the liver and kidneys, hemorrhage of the lungs, brain and myocardium, and hyperemia of the internal organs
		Rat	3 months, inhalation	NOEL = 16.5 mg/m^3 .
		Rat and Guinea Pig	6 months, inhalation	NOEL = 15 mg/m^3.
		Rat	Chronic, inhalation	A NOEL was not determined.
		Rat	Chronic inhalation	A NOEL was not determined.
		Rat	2.5 months, subcutaneous	reduced body weight gain.
5.5	Genetic Toxicity			
5.5.1	Bacterial Test	*Salmonella typhimurium* (strains TA1535, TA1537, TA98, TA100)	Ames assay	Negative +/- metabolic activation
		Salmonella typhimurium (strains TA98 and TA100)	Ames assay with modifications	Negative +/- metabolic activation
		Salmonella typhimurium (strains TA1535, TA1537, TA98, TA100, TA102, TA1538)	Ames assay	Negative +/- metabolic activation
		Photobacterium phosphorium	Mutatox™ Assay	Results were considered equivocal.
5.5.2	Non-bacterial in vitro Test	Rat hepatocytes and Chinese hamster embryo cells	DNA single-strand break assay	Negative
		HeLa Cells	Unscheduled DNA synthesis assay	Negative
		Human Lymphocytes	Chromosomal aberration assay	Negative
		Human Lymphocytes	Micronuclei assay	Negative
		Syrian Hamster Embryo	DNA amplification assay	Negative
		Mouse Lymphoma	Gene mutation assay	Negative
		Chinese Hamster Ovary	Chromosomal aberration assay	Negative
		BALB/c-3T3 Cells	Transformation assay	Indeterminate activity

5.5.3	Non-bacterial in vivo test	*Drosophila melanogaster*/ Canton-*S* males and *Basc* females.	Sex-linked reessive lethal assay	Negative
		Mouse	Micronuclei assay	Negative
		Mouse	Micronuclei assay	Positive
		Drosophila melanogaster	Sex-linked dominant lethal assay	Positive
5.6	Carcinogenicity	Rat and Mouse	2 year, oral diet	Negative in rats or female mice. An increase in lung tumors in male mice was considered equivocal.
5.7	Reproductive and Developmental toxicity	Rat	115 days, oral diet	NOEL =636 mg/kg (P1) NOEL = 152 mg/kg (F1)
		Rat	> 150 days, oral diet Parental effects: CD(M) CD(F) Wistar(M) Wistar(F) Reproductive: CD(M) CD(F) Wistar(M) Wistar(F) Offspring effects: CD(M) CD(F) Wistar(M) Wistar(F)	 NOAEL = 240 mg/kg NOAEL = 282 mg/kg NOAEL = 960 mg/kg NOAEL = 1219 mg/kg NOAEL > 2499 mg/kg NOAEL > 2783 mg/kg NOAEL > 2480 mg/kg NOAEL > .3018 mg/kg NOAEL = 240 mg/kg NOAEL = 282 mg/kg NOAEL = 960 mg/kg NOAEL = 1219 mg/kg
5.7.1	Reproductive toxicity: single generation reproductive toxicity study with teratology screen	No studies available		
5.7.2	Teratogenicity/Developmental Toxicity	Rat	Gestation, inhalation	No abnormalities were reported.
		Rat	7-16 day gestation, oral gavage	NOAEL >1,000 mg/kg.
		Rat	6-15 day gestation, inhalation	NOAEL >10 mg/m^3 TPA.
6.	Neurotoxicity	No studies available		
7.	Experience with Human Exposure	Human	Dermal	No irritant effects
		Human	Not reported	A Russian study reported no effects in workers exposed to high concentrations.
		Human	Not reported	A Russian study reported a moderate leukocytosis in workers involved in DMT synthesis.
7.1	Biological Monitoring	No studies available		
	Toxicodynamics and Toxicokinetics	Rat	5 day, oral diet	DMT is readily absorbed and primarily excreted by the kidney as terephthalic acid.
		Rat and Rabbit	The fate of a radiolabeled DMT was followed using ocular, dermal, oral, and intratracheal exposure routes.	DMT was not well absorbed by dermal, ocular, or even intratracheal exposures compared to oral. In all cases DMT was rapidly eliminated and primarily in urine.
		Rat and Mouse	Animals received a single oral dose of radiolabeled DMT. Feces and urine were collected over a 48-hour period.	90% was recovered in the urine and less than 1% was present in carcasses. In rats it was all terephthalic acid (TPA). In mice 70% was monomethyl terephthalate and

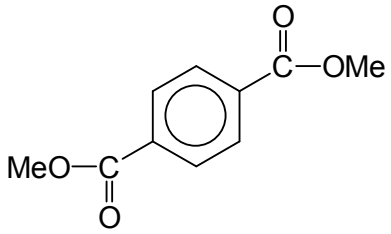
				30% was TPA.
		Rat	Animals were fed diets with 0, 1.0 or 2.0% DMT for 3 weeks.	Animals developed hypercalciuria and had urinary acidosis. DMT was metabolized to TPA.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 120-61-6
IUPAC Name: Dimethyl terephthalate
Molecular Formula: C10H10O4
Structural Formula:



Molecular Weight: 194.19
Synonyms: dimethyl 1,4-benzenedicarboxylate
dimethyl p-benzenedicarboxylate
dimethyl p-phthalate
methyl 4-carbomethoxybenzoate
methyl p-(methoxycarbonyl)benzoate
terephthalic acid, dimethyl ester

Physical description: white solid, or colorless molten Liquid

1.2 Purity/Impurities/Additives

Degree of purity: 99.9% minimum

Major impurities: Methyl (p-formyl)benzoate – 40 ppm max.

Methyl hydrogen terephthalate – 225 ppm max.

Essential additives: None

1.3 Physico-Chemical properties

Water solubility: 19 mg/L (25^{o} C);

Partition coefficient: logP = 2.25; P = 178

Vapor pressure: 0.01 mm Hg 25°C

Melting point: 141^{o} C (286^{o} F)

Flash point: 153^{o} C (308^{o} F)

Biodegradation: Readily biodegradable

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

Production Volume

Total annual North American nameplate (maximum capacity) production capacity is estimated for 2004 at 1,917,000 mt or 4.23E9 pounds (SRI Consulting Jan. 2000).

Total annual worldwide nameplate production capacity is estimated for 2004 at 4,936,000 mt or 1.09E10 pounds (SRI Consulting Jan. 2000).

Manufacturing Process

In the United States, dimethyl terephthalate (DMT) is manufactured by the air oxidation of p-xylene in an enclosed continuous process. It is purified by distillation and transferred through closed lines and stored in tanks as a molten liquid.

Use

Dimethyl terephthalate is used as an industrial intermediate to manufacture polyethylene terephthalate (PET) and dioctyl terephthalate. A good proportion of these end-uses occur at the same plant site as its initial synthesis. Some DMT is sold to other producers, also for the manufacture of polyethylene terephthalate. Transfer to other plant sites is as the molten liquid in tank cars or trucks.

Form of marketed product

Molten liquid

2.2 Environmental Exposure and Fate

2.2.1 Releases and Sources

The primary source of release is permitted stack air emissions and possible fugitive air emissions. These emissions, while not measured, are believed to be low as a result of the limited volatility of DMT. Emissions to waterways, which also are not measured, are also believed to be negligible. In the U. S., DMT is not listed as a Toxic Release Inventory (TRI) chemical under EPCRA 313, or as a Hazardous Air Pollutant. Aqueous waste streams from the manufacturing and use processes are sent to on-site corporate waste-water treatment facilities for biooxidation prior to release into public waterways. Because DMT has limited water solubility and is readily biodegradable, any DMT released from the on-site waste-water treatment systems to waterways is believed to be negligible. Organic waste streams from the manufacturing and use processes are incinerated.

Fugitive Emissions

Although fugitive emissions have not been determined, such emissions are expected to be low. Manufacture, use and storage as an industrial intermediate take place within closed continuous equipment and DMT has very limited volatility.

2.2.2 Environmental Fate

Dimethyl terephthalate is a solid with limited vapor pressure (100 mmHg at 208^{o} C; 0.01 mmHg at 25^{o} C; 1.15 mmHg at 93^{o} C) and low water solubility (28.7 mg/L (20^{o} C); 19 mg/L (25^{o} C); 37.2

mg/L (25^{o} C). When DMT was placed in wastewater it was readily degraded by microbes (BOD reduced up to 95% in 48-hours), and when mixed with sludge, it had a theoretical BOD of 84% (MITI, 1992). When DMT was placed in secondary wastewater, an IC_{50} was determined to be >5000 mg/L (DMT was in a suspension). Because DMT biodegrades readily, it is expected to partition primarily to water and soil, where it will biodegrade and not persist or bioaccumulate (logP = 2.25). Bioconcentration and absorption to sediment are also not expected to be very important fate processes in aquatic environments (log BCF = 1.21 and Koc = 2.49). Dimethyl terephthalate has a photooxidation half-life of 4.7 to 46.6-days (Howard, *et al*.)

If released into water, DMT is expected to degrade by simple hydrolytic processes with half lives of 321-days at neutral pH (Mabey and Mill, 1978). It has an estimated half-life of 1-4 weeks for surface water and 2-8 weeks for ground water (Howard, *et al*.). In studies with river water, 50 ppm of DMT were degraded in 3-days (Kondo, *et al*., 1988).

If released into air, vapor phase DMT will react with photochemically-produced hydroxyl radicals and have an estimated half-life of approximately 5 to 47-days (Howard, *et al*.).

Environmental Partitioning

An EPIWIN Level III Fugacity Model was run using a log Kow=2.25, Henry's Law Constant of 0.000134 atm*m^3/mol, vapor pressure of 0.01 mmHg, melting point of 141°C, soil Koc of 72.9, and the default of equal distribution between compartments. The results show that DMT is expected to partition primarily to soil and water.

Compartment	Percent
Air	13.9
Water	34.4
Soil	51.6
Sediment	0.134

2.2.3 Predicted Environmental Concentration

Concentrations of DMT in the environment have not been monitored, but would be expected to be low. A Predicted Environmental Concentration (PEC) has not been calculated, since releases to water are expected to be insignificant due to its biooxidation in waste-water and current manufacturing processing in the U.S.

2.3 Human Exposure

2.3.1 Occupational Exposure

Less than 500 workers are estimated to be exposed at approximately 5-6 manufacturing and use sites in the U.S. Exposure may occur primarily during quality control sampling, loading or unloading tank cars or trucks, or when lines are disconnected for maintenance. Actual exposure is limited, because manufacturing and use processes are enclosed and continuous. Most manufacturing facilities (columns, tanks, lines) are located out-of-doors, with the processes being controlled in-doors via computer. Inhalation exposure is minimal, because of the very limited volatility, and for short periods (sampling, etc.). Accidental dermal contact is of concern primarily because of possible burns from molten liquid (melting point of 141 C^{o}). The use of personal

protective equipment (safety glasses, cap and leather gloves) is required whenever dermal exposure might occur.

2.3.2 Consumer Exposure

Since DMT is used solely as an industrial intermediate, no significant consumer exposure is anticipated.

2.3.3 Indirect Exposure via the Environment

Due to the low volatility of DMT and the manner in which it is produced and utilized, i.e., closed systems on-site industrial intermediate, exposure to non-industrial workers is essentially zero. Exposure through water is also of extremely low likelihood, as DMT is not utilized in consumer products. Furthermore, the amounts released into water from industrial sites are very low and DMT is readily degraded and does not bioaccumulate in aqueous organisms that could be consumed.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

Analog Justification

Data for dimethylterephthalate (DMT) is available for all SIDS health endpoints. However, for reproductive and developmental toxicity, the available data on DMT is not considered sufficient to support a conclusion that these endpoints have been completed. As a result, additional data from terephthalic acid (TPA) is being presented to support the conclusion that the reproductive and developmental toxicity endpoints have been completed. The use of TPA data for health endpoints is acceptable due to the principle that DMT metabolizes to form TPA.

3.1.1 Toxicokinetics, Metabolism and Distribution

Several studies conducted in rats, rabbits, and mice have all indicated that DMT is readily absorbed from the digestive tract and rapidly eliminated in the urine within 48-hours (Haskell Laboratory; Moffitt, A.E. Jr., et al., 1975; Heck, H. d.'A., 1980). Most of the absorbed DMT is metabolized to terephthalic acid (TPA) via hydrolysis, which sometimes combines with calcium to form TPA-Ca^{++} precipitates. In mice, the predominate metabolite was monomethyl terephthalate.

3.1.2 Acute Toxicity

Dimethyl terephthalate is of low toxicity following oral, inhalation, and dermal exposures. The oral LD_{50} in rats ranged from 4,390 to >6,590 mg/kg (Marhold, J.V., 1972; Krasavage, et al., 1973). Clinical signs consisted of slight to moderate weakness at all doses and slight tremors and atoxia at the highest doses (5,020 and 6,590 mg/kg). Respiratory irritation, mucosal hyperemia, increased excitation upon stimiulation, irregular breathing, and cyanosis were noted in rats following exposure to a hot vapor (LC_{50} >6 mg/L) (Sanina, Y.P. and Kochetkova, T.A., 1963). No deaths were reported in guinea pigs following dermal exposure to 5,000 mg/kg (Patty's Ind. Hyg. Tox., 1981).

3.1.3 Irritation

DMT applied topically to guinea pigs, mice (tails dipped into DMT solutions), and rabbits, was reported to be slightly irritating (Eastman Kodak, 1957; Eastman Kodak, 1963; Sanina, Y.P. and Kocketkova, T.A., 1963). In 2 different studies, DMT instilled in rabbit eyes had either no effect or induced a mild irritation (Eastman Kodak, 1957; Anonymous, 1986). A third study indicated a pronounced conjunctivitis was induced (time for return to normal was not reported) (Kamal' Dinova, Z.M., et al., 1962).

3.1.4 Sensitisation

Three different studies have all concluded that DMT does not induce allergic contact sensitization (Krasavage, W.J., et al., 1973; Patty's Ind. Hyg. Tox., 1981).

3.1.5 Repeated Dose Toxicity

Species* / Duration / Exposure Route	Dose / Exposure Level	NOEL/NOAEL	Reference
14 Days / Gavage	5,000 mg/kg/day	Not Determined.	Haskell Laboratory, MR-423-1.
14 Days / Diet	0, 0.5, 1.0, 1.5, 2, or 3% or 0, 5000, 10000, 15000, 20000, or 30000 ppm (Avg. dose for males was 660, 1320, 1890, 2260, and 2590 mg/kg/day, for females it was 638, 1277, 1790, 2290, and 3020 mg/kg/day.)	NOEL of 0.5% (660 mg/kg) in males and 1.0% (1277 mg/kg) in females	Chin, T.Y. *et al*., 1981
16 Days / Diet	5% or 10%	Not Determined	Haskell Laboratory, MR-423-1.
28 Days / Diet	0 or 5% or 50000 ppm(3,750 mg/kg/day)	Not Determined	Patty's Ind. Hyg. & Tox., 3rd Ed.
35-39 Days / Diet	500 mg/kg/day	NOEL was 500 mg/kg.	Prusakov, V.M., 1966
13 Weeks / Diet	0.5, 1.6 or 3% or 5000, 16000, or 30000 ppm	Not Determined	Vogin, E. E., 1972
13 Weeks / Diet	0.175, 0.25, 0.5, 1.0 or 2.0% or 1750, 2500, 5000, 10000, or 20000 ppm	A NOAEL of 0.5% for rats and 2.0% for mice.	Federal Register, 1981
96 Days / Diet	0, 0.25, 0.5 and 1.0% or 2500, 5000 or 10000 ppm (Avg. dose was 152, 313, and 636 mg/kg/day)	NOEL was 0.5% (313 mg/kg)	Krasavage, W.J., *et al*., 1973.
5 Months / Inhalation	1-4 or 40-70 mg/m^3 of DMT	Not Determined	Sanina, Y.P., 1963.
3 Months / Inhalation	0.0, 16.5, and 86.4 mg/m^3	NOAEL was 86.4 mg/m^3	Krasavage, W.J., *et al.*, 1973.
6 Months / Inhalation	15 mg/m^3	NOEL was 15 mg/m^3	Lewis, T.R. *et al*., 1982.
"Chronic" / Inhalation	0.08, 0.4 or 1 mg/m^3	Not Determined	Davidenko, A.V. *et al*., 1982.
"Chronic" / Inhalation	0.08, 0.4 or 1 mg/m^3	Not Determined	Davidenko, A.V. *et al*., 1984.
10 Days and 2.5 Months / Subcutaneous	2 g/kg (10 days) 1 g/kg (2.5 months)	NOEL was 2 g/kg	Slyusar, M.P., 1964.

* All studies were conducted in rats, while the NCI study also included mice and the Lewis study also included guinea pigs.

Numerous studies, mostly using rats, have been conducted to evaluate the affects of DMT following repeat exposures from various administration routes including oral (gavage and dietary), inhalation, and subcutaneous injections. Oral exposure studies have ranged in length from 2 to 13 weeks. Inhalation exposure studies of DMT dust have been conducted for up to 6 months in duration with a NOEL of 15 mg/m^3 (highest level evaluated) without evidence of any types of effect (Lewis, T.R. *et al*., 1982). The only target organ identified in oral exposure studies was that of the urinary tract. However, the observed toxicity was not the result of a direct DMT effect, but was mediated through indirect mechanisms. When DMT is administered in high doses it may induce the formation of renal and bladder crystals and calculi. The mechanism by which this occurs is through its metabolism to terephthalic acid (TPA) and the formation of TPA-Calcium precipitates. The

physical presence of these crystals and calculi leads to hematuria and to thickening of the bladder wall. The minimum dose level and exposure length at which these effects have been reported are 1.5% (1890 mg/kg; NOEL was 1790 mg/kg) and greater dietary concentrations for 14 days (Chin, T.Y. *et al*., 1981). Crystals were noted as being present in 12/16 males and 6/16 females fed DMT in their diet at a level of 3% for 28 days (Vogin, E. E., 1972). However, and for reasons that are unknown, crystal formation and hematuria are not consistently observed in all repeat dose studies. It was not noted in a 14-day gavage exposure study at 5,000 mg/kg (Haskell Laboratory), in two different studies of at least 28 days with dose levels of 5% (diet; Patty's Ind. Hyg. & Tox., 3rd Ed.) or 500 mg/kg (gavage) (Prusakov, V.M., 1966), or in two 13-week studies with maximum dietary exposure levels of either 1.0 or 2.0% (Krasavage, W.J., *et al.*, 1973, and Federal Register 1981). In addition, this phenomenon was not observed in the 2-year carcinogenicity study where DMT was present in the diet at 2.5 and 5% (Federal Register, 1981). The primary effect noted in these latter oral studies that did not develop calculi, or from administering DMT via other exposure routes, was a nonspecific decrease in body weight gain without any histological evidence of toxicity.

3.1.6 Mutagenicity

The results from several bacterial mutagenicity assays (Ames) have all indicated DMT is not mutagenic (Zeiger, E., et al., 1982; Zieger, E., et al., 1985; Kozumbo, W.J., et al., 1982; Monarca, S., et al., 1991; Monarca, S., et al., 1989; Elmore, E. and Fitzgerald, M.P., 1990). Negative results were also the norm in *in vitro* DNA single-strand breakage assays, unscheduled DNA synthesis test, sister chromatid exchange assay, and in an assay evaluating the formation of micronuclei (Monarca, S., et al., 1989; Monarca, S., et al., 1991; Loveday, K.S., et al., 1990). These studies utilized mouse hepatocytes, Chinese hamster embryo cells, HeLa cells, and human lymphocytes. Negative in vivo studies include a sex-linked recessive lethality tests in *Drosophila* and one of two micronuclei studies in mice (Foureman, P., et al., 1994; Shelby, M.D., et al., 1993). The significance of an increase in micronuclei formation in one of these two *in vivo* tests is questionable due to many irregularities in the study's methodology as well as evidence of toxicity from the vehicle (see dossier for full discussion) (Goncharova, R.I., *et al.*, 1988).

3.1.7 Carcinogenicity

DMT was evaluated for carcinogenic potential in a 2-year bioassay (Federal Register, 1981). This study, conducted by the National Cancer Institute of the United States, evaluated DMT dietary exposure levels of 2.5 and 5.0% (2,500 and 5,000 ppm) in rats and mice. These exposure levels did not affect body weight or survival, or induce any clinical signs of toxicity. No increases in tumors were noted in rats of either sex or female mice. An increase in lung tumors in male mice was considered equivocal.

3.1.8 Toxicity for Reproduction

Effects on Fertility

Reproductive toxicity was evaluated by exposing male rats to diets containing 0.25, 0.50, or 1.0% DMT for 115 days (Krasavage, W.J., *et al.*, 1973). These males were then mated with females that had been on the DMT diet for 6 days. After mating, females remained on the diet through lactation. No signs of toxicity were observed in either the male or female parental animals. Pups born to parents fed 0.5 and 1.0% DMT had significantly lower average body weights at weaning when compared to the controls. The NOEL was 1.0% (636 mg/kg/day) for parents and 0.25% (152 mg/kg/day) for their offspring. This effect on the offspring was likely due to exposure to DMT through lactation and having access to the mother's food, and hence it is a primary toxicity from DMT exposure. In a one-generation reproduction study, no adverse effects on fertility were noted

in adult rats fed up to 5% terephthalic acid (TPA) in the diet (CIIT 1982). Both maternal and post-natal effects occurred in the 2% and 5% groups. The NOAEL for maternal toxicity and for the F1 offspring was 0.5% (240 to 307 mg/kg), while the NOAEL for reproductive effects was >5.0% (2480-3018 mg/kg) TPA in the diet. There were increased postnatal deaths on Day 1 (fetotoxicity) and decreased survivability to Day 21. Several large litters of pups were lost to dams suffering obvious signs of maternal toxicity. Several of these dams did not allow the pups to nurse or attend to the litters. Unscheduled deaths occurred during the postweaning period in the 5% groups and was associated with a very high incidence of renal and bladder calculi. Weanling animals exhibit a higher incidence of calculi compared to adults consuming the same dietary level of terephthalic acid. This can be explained by the large amount of feed consumed in relation to body weight for young animals experiencing their initial growth spurt. Weanling animals are not more sensitive to TPA toxicity when the results are expressed on a mg/kg basis.

Developmental Toxicity

The potential for DMT to induce developmental toxicity in rats has been evaluated following an inhalation exposure to DMT at 1 mg/m^3 and after gavage exposure to 1,000 mg/kg throughout gestation (Krotov, Y.A. and Chebotar, N.A., 1972, and Hoechst 1986). In addition, inhalation exposures to terephthalic acid (TPA), the primary metabolite of DMT, at exposure levels up to 10 mg/m^3 have been assessed during days 6-15 of gestation in rodents (Amoco Corporation, 1989 and Ryan, *et al.*, 1990). No abnormal developmental effects and no pre- or post-implantation losses were noted in any study.

3.1.9 Experience with Human Exposure

There were only a few isolated reported instances in the literature in which possible effects from DMT exposure to humans were evaluated. In one, an oily paste containing 80% DMT showed no irritant effects 24 hours after 10 applications to human skin (Massmann, W., 1966). In another, no adverse effects were reported in workers exposed to high concentrations of DMT (Korbakova, A.I., 1964). While in a third study, a moderate leukocytosis was found in workers involved in the synthesis of DMT (Kamal'dinova, Z.M., et al., 1962). However, it was noted that these workers were also exposed to other chemicals.

3.2 Initial Assessment for Human Health

Workers

Airborne emissions consist primarily of dust or fumes. Product is normally handled in closed systems at all times. Air concentrations are predominately under 0.3 mg/m^3, higher air levels are associated with clean up and require use of respiratory protection devices. [0.3 mg/m^3 was the TWA value of twelve workers completing a full shift. Measured values ranged from 0.15 to 0.99 mg/m^3.]

Consumers

There is no known direct consumer exposure. Dimethyl terephthalate is used solely as an industrial intermediate. Residual DMT at an average of less than 1 ppm is found within polyethylene terephthalate (PET). DMT is esterified with ethylene glycol prior to incorporation into PET. This esterification process results in essentially no measurable DMT in finished product.

Those Exposed to the Environment

Based on the fact that DMT is an industrial intermediate manufactured and used in enclosed equipment with very low volatility, and is readily biodegradable, there is a very low potential for appreciable environmental exposure.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Acute toxicity studies to aquatic organisms indicate DMT is moderately toxic. Fish (Fathead minnow) had a 96h LC_{50} of 9.6 mg/L, in invertebrates it was 30 mg/L in *Daphnia,* >30 mg/L in the Sideswimmer (48h), >100 mg/L in the Flatworm (96h), and >30 mg/L in the snail (96h) (Eastman Kodak Co. 1977 and 1984). Similar toxicity values were seen in an acute algal toxicity study (72h NOEC 10.8 mg/L, biomass 72h EC_{50} 27.6 mg/L and growth 72h EC_{50} >32.3 mg/L) (Huls AG, 1993). Chronic toxicity studies were not available on any species.

The Predicted No Effect Concentration (PNEC) value for the aquatic environment would likely be 96 ug/L. The PNEC was estimated by applying a 100-fold safety factor to the most sensitive species (Fathead minnow; LC_{50} = 9.6 mg/L).

4.2 Terrestrial Effects

Based on its physical and chemical properties, DMT is not expected to accumulate in terrestrial environments. Although some soil bacteria were unable to catabolize DMT, most studies with soil microorganisms indicated that it could be used as a carbon source. If DMT is released into soil, it should have medium to high soil mobility.

Studies have been conducted assessing DMT effects on plant germination and seedling growth (Eastman Kodak Co. 1976 and 1984). Results showed that DMT had no effect on seed germination rates in lettuce at 1 mg/L, or in ryegrass and radish at 10 mg/L (Another study showed no effects in lettuce or radish at 30 mg/L). There was no effect on corn, marigold, and lettuce seedlings following exposure to DMT at concentrations of 33 mg/L, or on radish seedlings at 10 mg/L (Another study showed no effects on corn at 100 mg/L and radish, marigold, and lettuce at 1000 mg/L). It is important to point out that the robustness of the information associated with these studies questions their validity and overall usefulness.

4.3 Initial Assessment for the Environment

Aquatic Compartment

DMT is minimally soluble in water and has an overall low hazard potential in aquatic environments. Due to its main use as an industrial intermediate in the production of polymers, negligible quantities are released. Any DMT that does end up in this compartment has a very low potential to accumulate as it is readily removed through direct hydrolysis and microbial degradation (see 3.1.1). If a large quantity of material is accidentally released into the environment, it could lead to adverse consequences to some aquatic organisms. Both fish (Fathead minnow) and invertebrates (daphnia and sideswimmer) showed a moderate level of toxicity to it in lethality testing. Effects on algal growth were also noted at similar concentrations.

Terrestrial Compartment

Annual land releases of DMT from its manufacturing sites are essentially zero due to its end use as an industrial intermediate. Any material that does end up in terrestrial environments will be readily degraded through hydrolytic processes or be broken down by microbes. DMT had negligible effects on seed germination rates and seedling growth. Thus, DMT presents a very low concern in the terrestrial environment.

Atmospheric Compartment

Although atmospheric emissions have not been determined, such emissions are expected to be low. DMT's manufacture, use, and storage as an industrial intermediate take place within closed continuous equipment and DMT has very limited volatility. Available data indicate that vapor phase DMT will react with photochemically-produced hydroxyl radicals and lead to its removal. Thus, DMT presents a very low concern in the atmospheric environment.

5 CONCLUSIONS AND RECOMMENDATIONS

Conclusions

Dimethyl terephthalate is a high production volume chemical. It is produced in closed continuous equipment systems and is used primarily within its own manufacturing facilities in the synthesis of polyethylene terephthalate plastic and, to a lesser extent, dioctyl terephthalate. There is no known use of DMT in consumer or commercial products. When transported, it is shipped in bulk containers as a molten liquid. Thus, human exposures are very minimal and limited. The main exposure concern is that of direct physical burns due to accidental contact to molten DMT.

The physical-chemical properties of DMT which include a slow hydrolysis, photo-oxidation half-life of weeks, and stability in surface and ground water with half-lives of weeks, indicate this chemical is persistent enough in the environment to have a potential for causing an environmental hazard if there was the potential for significant environmental releases. This chemical is moderately toxic to fish, daphnid, and green algae. However, it is not expected to bioaccumulate in fish and is not expected to biomagnify via food chains.

Results from acute and repeat dose studies indicate DMT is of a low order of toxicity. In addition, given the weight of the evidence, DMT does not appear to be mutagenic or genotoxic, nor was it deemed to be a carcinogen based on 2-year feeding studies. Studies on DMT and the metabolite TPA indicate no evidence of developmental or reproductive toxicity. The primary toxicity manifested in laboratory animals was due to a secondary effect from its metabolism to TPA and the subsequent formation of renal crystals or calculi. Based on urinary solubility of Ca-TPA, human urine would become saturated with Ca-TPA at a TPA concentration of approximately 8-16 mM. Assuming an average urine volume formation of 1.5 L/day and that DMT is metabolized solely to TPA. The amount of DMT that would have to be absorbed in order to achieve a concentration of 8 mM in 1.5 L of urine, is 2,400mg/day (Heck, H. d'A. and Tyl, R.W., 1985; mw=194.2 x 8 mM x 1.5 L urine/day).

Recommendations

It is recommended that DMT be considered as low priority for further work.

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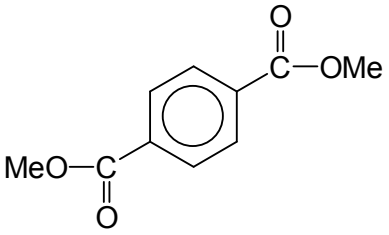
SIDS DOSSIER

Dimethyl terephthalate

CAS No. 120-61-6

Sponsor Country: United States

SIDS PROFILE

1.01 A.	**CAS No.**	120-61-6
1.01 C	**CHEMICAL NAME**	Dimethyl Terephthalate
1.01 D.	**CAS DESCRIPTOR**	
1.01 G.	**STRUCTURAL FORMULA**	
	OTHER CHEMICAL IDENTITY INFORMATION	
1.5	**QUANTITY**	
1.7	**USE PATTERN**	Used only as an industrial intermediate for the manufacture of polyethylene terephthalate and dioctyl terephthalate
1.9	**SOURCES AND LEVELS OF EXPOSURE**	(a) Human exposure is limited primarily to the workplace and can occur during sampling. (b) Environmental releases are low as a result of bulk storage and handling, closed system manufacture and use, and handling as a molten liquid with very low vapor pressure.
ISSUES FOR DISCUSSION (IDENTIFY, IF ANY)	SIDS testing required: None.	

SIDS SUMMARY DATA

CAS NO: 120-61-6		Information	OECD Study	GLP	Other Study	Estimation Method	Acceptable	SIDS Testing Required
STUDY		Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
PHYSICAL-CHEMICAL DATA								
2.1	Melting Point	Y	N	N	Y	N	Y	N
2.2	Boiling Point	Y	N	N	Y	N	Y	N
2.3	Density	Y	N	N	Y	N	Y	N
2.4	Vapor Pressure	Y	N	N	Y	N	Y	N
2.5	Partition Coefficient	Y	N	N	Y	N	Y	N
2.6	Water Solubility	Y	N	N	Y	N	Y	N
	pH and pKa values	NA	NA	NA	NA	NA	NA	NA
2.12	Oxidation: Reduction potential	NA	NA	NA	NA	NA	NA	NA
OTHER P/C STUDIES RECEIVED								
ENVIRONMENTAL FATE and PATHWAY								
3.1.1	Photodegradation	Y	N	N	Y	N	Y	N
3.1.2	Stability in water	Y	N	N	Y	N	Y	N
3.2	Monitoring data	N	N	N	N	N	N	N
3.3	Transport and Distribution	Y	N	N	Y	Y	Y	N
3.5	Biodegradation	Y	N	N	Y	Y	Y	N
OTHER ENV FATE STUDIES RECEIVED								
ECOTOXICITY								
4.1	Acute toxicity to Fish	Y	N	N	Y		Y	N
4.2	Acute toxicity to Daphnia	Y	N	N	Y		Y	N
4.3	Toxicity to Algae	Y	N	Y	Y		Y	N
4.5.2	Chronic toxicity to Daphnia	N						N
4.6.1	Toxicity to Soil dwelling organisms	N						N
4.6.2	Toxicity to Terrestrial plants	Y	N	N	Y		Y	N
4.6.3	Toxicity to Birds	N						N
OTHER ECOTOXICITY STUDIES RECEIVED								

TOXICITY								
5.1.1	Acute Oral	Y	N	N	Y		Y	N
5.1.2	Acute Inhalation	Y	N	N	Y		N	N
5.1.3	Acute Dermal	Y	N	N	Y		Y	N
5.4	Repeated Dose	Y	N	N	Y		Y	N
5.5	Genetic Toxicity in vitro	Y	N	N	Y		Y	N
	Gene mutation	Y	N	N	Y		Y	N
	Chromosomal aberration	Y	N	N	Y		Y	N
5.6	Genetic Toxicity in vivo	Y	N	N	Y		Y	N
5.8	Reproduction Toxicity	Y	N	N	Y		Y	N
5.9	Development/Teratogenicity	Y	N	N	Y		N	N
5.11	Human Experience	Y	N	N	Y		Y	N
OTHER TOXICITY STUDIES RECEIVED								

1.01 SUBSTANCE INFORMATION

A. CAS-Number **120-61-6**

B. Name (IUPAC name) 1,4-Benzenedicarboxylic acid, dimethyl ester

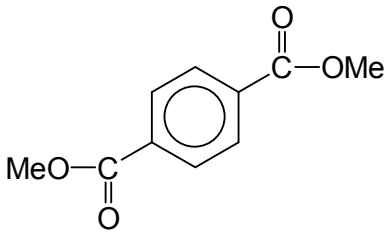
C. Name (OECD name) Dimethyl terephthalate

D. CAS Descriptor (where applicable for complex chemicals) Not applicable in this case

E. EINECS-Number **204-411-8**

F. Molecular Formula **$C_{10}H_{10}O_4$**

G. Structural Formula (indicate the structural formula in smiles code, if available**)**



H. Substance Group (if possible, only for petroleum products, see HEDSET Explanatory note)

Not Applicable

I. Substance Remark (indicate the substance remark as prescribed in the EINECS Inventory, if possible)

J. Molecular Weight 194.19

1.02 OECD INFORMATION

A. Sponsor Country: United States of America

B. Lead Organization U.S. Environmental Protection Agency

Contact person: Mr. Oscar Hernandez
Director, Risk Assessment Division

Address: Office of Toxic Substances (7403)
U S Environmental Protection Agency
401 M Street SW
Washington, DC 20460
Telephone (202) 260-1835
Fax (202) 260-1216

C. Name of responder (Information on a responder should be provided when companies respond to Lead Organization or SIDS Contact Points)

Name: James A. Deyo D.V.M., Ph.D., D.A.B.T.
Technical Associate
Product Safety and Stewardship
Address: Eastman Chemical Company
Kingsport, TN 37662-5280

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance
Element [ ]; inorganic [ ]; natural substance [ ]; organic [X]; Organometallic [ ]; petroleum product [ ]

B. Physical State (at 20^{o} C and 1.013 hPa)
Gaseous [ ]; liquid [ ]; solid [X]

C. Purity (indicate the percentage by weight/weight)
99.9% (Eastman Chemical Company)

1.2 Synonyms

dimethyl 1,4,-benzenedicarboxylate
dimethyl p-benzenedicarboxylate
dimethyl p-phthalate
methyl 4-carbomethoxybenzoate
methyl p-(methoxycarbonyl)benzoate
terephthalic acid, dimethyl ester
DMT

1.3 IMPURITIES (indicate CAS No., chemical name (IUPAC name is preferable), percentage, if possible EINECS number)

(a) Methyl (p-formyl) benzoate – max. specification limit 40 ppm

(b) Methyl hydrogen terephthalate – max. specification limit 225 ppm

1.4 ADDITIVES (e.g. stabilizing agents, inhibitors, etc. Indicate CAS No. chemical name (IUPAC) name is preferable), Percentage, if possible EINECS Number), the component of The UVCB (Substance with no defined composition) should Be indicated here)

None

1.5 QUANTITY (Information on production or import levels should be provided in Figures or ranges (e.g., 1,000-5,000, 5,000-10,000 tonnes, etc.) per responder or country and the date for which those ranges apply should be given. For EEC Member states only indicate the Community import figure. Give an estimation of the global production quantity

in the remarks field. Information on the number of producers in the country and the source of information should also be described in the remarks field)

Total annual North American nameplate (maximum capacity) production capacity is estimated for 2004 at 1,917,000 mt or 4.23E9 pounds (SRI Consulting Jan. 2000).

Total annual worldwide nameplate production capacity is estimated for 2004 at 4,936,000 mt or 1.09E10 pounds (SRI Consulting Jan. 2000).

1.6 LABELLING AND CLASSIFICATION (If possible, enter information on labeling and classification such as labeling and classification system, existence of specific limit, symbols, nota, R-Phrases and S-Phrases of EC Directive 67/548/EEC, See HEDSET Explanatory note.)

1.7 USE PATTERN

A. General

Type of Use: Industrial intermediate used to manufacture polyethylene terephthalate, and dioctyl terephthalate

Category: Non-dispersive use; Chemical industry use as intermediate

B. Uses in Consumer Products

None

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

ACGIH: None

1.9 SOURCES OF EXPOSURE

Dimethyl terephthalate is manufactured from the oxidation of p-xylene by an enclosed, continuous process. It is handled as a molten liquid, possessing low vapor pressure, transferred through closed lines to heated storage tanks. Transport of molten DMT is via tank car or truck. DMT is reacted further on site or other industrial sites to manufacture polyethylene terephthalate polyester and dioctyl terephthalate.

There is limited potential for industrial exposure, which would occur primarily during quality control sampling. Short periods (one worker per day at one plant up to one- hour per 8-hour shift) of exposure to vapor can also occur during the loading of trailers and tank cars. The primary dermal hazard would be thermal burns from the hot molten DMT during sampling or line disconnection. The required wearing of leather gloves during these operations minimizes the possibility of dermal contact and burns.

Because DMT is handled as a melt with low vapor pressure in enclosed manufacturing, storage and processing systems the potential for environmental release is limited.

2.1 MELTING POINT: 141° C (286° F)
Method:
GLP: Yes [ ]
No [X]
Comments: Information predates GLP regulations
Reference: Dimethyl terephthalate, BG Chemie Toxicological Evaluations 1 Potential Health Hazards of Existing Chemicals, Springer-Verlag, Berlin Heidelberg New York London Paris Tokyo Hong Kong Barcelona

2.2 BOILING POINT: 280° C (543° F); 288° C (550° F)
Method:
GLP: Yes [ ]
No [X]
Comments: Information predates GLP regulations
Reference: 1.) Dimethyl terephthalate, BG Chemie Toxicological Evaluations 1 Potential Health Hazards of Existing Chemicals, Springer-Verlag, Berlin Heidelberg New York London Paris Tokyo Hong Kong Barcelona
2.) The Merck Index (12) and USEPA OPPT/ICB internal database

2.3 SPECIFIC GRAVITY (water = 1): 1.1 – solid; liquid (molten) 1.05

Method:
GLP: Yes [ ]
No [X]
Comments: Information predates GLP regulations
Reference: Material and Safety Data Sheet; Eastman Chemical Company

2.4 VAPOR PRESSURE: 133 mbar (100 mmHg) at 208° C; 1.15 mmHg at 93° C; 0.01 mmHg at 25° C
Method:
GLP: Yes [ ]
No [X]
Comments: Information predates GLP regulations
Reference: 1.) Material and Safety Data Sheet; Eastman Chemical Company
2.) Aldrich MSDS found ONLINE
3.) USEPA OPPT/ICB internal database

2.5 PARTITION COEFFICIENT: logP = 2.25; P = 178
Method:
GLP: Yes [ ]
No [X]
Comments: Obtained from HSDB No. 2580

Reference: Hansch, C., Leo, A., D. Hoekman. (1995) Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society; 69.

2.6 WATER SOLUBILITY:

A. Solubility: 1.) 28.7 mg/L (20° C); 2.) 19 mg/L (25° C); 3.) 140 mg/L (25° C); 4.) 500 mg/L (20° C); 5.) 37.2 mg/L (25° C)

Method: 1.) EEC A6-MOS/PHC/019
GLP: Yes [X]
No [ ]
Comments: Methods used for studies 2-5 are unknown or are believed to be estimations.
Reference: 1.) Montefibre Spa; IUCLID
2.) Kuhne, R. *et al.* (1995) Chemosphere 30:2061-77 ; HSDB No. 2580.
3.) USEPA OPPT/ICB EPIWIN
4.) Dimethyl terephthalate, BG Chemie Toxicological Evaluations 1 Potential Health Hazards of Existing Chemicals, Springer-Verlag, Berlin Heidelberg New York London Paris Tokyo Hong Kong Barcelona
5.) Eastman Kodak Company Environmental Safety Data Sheet; HAEL No. 77-0311 and 80-0056; unpublished data.

B. pH Value, pKa Value: NA

2.7 FLASH POINT: 153° C (308° F)

Method: Cleveland, open cup
GLP: Yes [ ]
No [X]
Comments: Information predates GLP regulations
Reference: Material and Safety Data Sheet; Eastman Chemical Company

2.8 AUTOIGNITION TEMPERATURE: 519° C (965° F)

Method: ASTDM D-2155
GLP: Yes [ ]
No [X]
Comments: Information predates GLP regulations
Reference: Material and Safety Data Sheet; Eastman Chemical Company

2.9 FLAMMABILITY: Non-flammable

2.10 EXPLOSIVE PROPERTIES

A. **Sensitivity to mechanical impact:** Insensitive
Method:
GLP: Yes [ ]
No [X]
Comments: Information predates GLP regulations
Reference: Material and Safety Data Sheet; Eastman Chemical Company

B. **Lower explosive limit:** 0.000033 mg/L
Method:
GLP: Yes [ ]
No [X]
Comments: Information predates GLP regulations
Reference: Material and Safety Data Sheet; Eastman Chemical Company

2.11 OXIDIZING PROPERTIES: Not an oxidizer

2.12 OXIDATION/REDUCTION POTENTIAL

N/A

2.13 ADDITIONAL DATA

A. **Physical Form:** Solid; Liquid (molten)

Method:
GLP: Yes [ ]
No [X]
Comments: Information predates GLP regulations
Reference: Material and Safety Data Sheet; Eastman Chemical Company

B. **Color:** White

Method:
GLP: Yes [ ]
No [X]
Comments: Information predates GLP regulations
Reference: Material and Safety Data Sheet; Eastman Chemical Company

C. Odor: Slight

Method:
GLP: Yes [ ]
No [X]
Comments: Information predates GLP regulations
Reference: Material and Safety Data Sheet; Eastman Chemical Company

D. Vapor density (Air = 1): 6.7

Method:
GLP: Yes [ ]
No [X]
Comments: Information predates GLP regulations
Reference: Material and Safety Data Sheet; Eastman Chemical Company

3.1 STABILITY

3.1.1 PHOTODEGRADATION

A. **Test substance:** Dimethyl terephthalate
Test type: Hydroxyl radical and ozone reactivity
Test method:
GLP: Yes [ ]
No [X]
Test result: DMT was reactive toward OH• radicals with a half-life of approx. 3-days, and was unreactive toward ozone.
Comments: The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.
Reference: Brown, S.L., *et al*., 1975.

B. **Test substance:** Dimethyl terephthalate
Test type: Photooxidation half-life
Test method:
GLP: Yes [ ]
No [X]
Test result: The half-life was determined to be 4.7 to 46.6-days.
Comments: The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.
Reference: Howard, P.H., *et al*., Page 465.

3.1.2 STABILITY IN WATER

A. **Test substance:** Dimethyl terephthalate
Test type: Alkoxyradical reactivity
Test method:
GLP: Yes [ ]
No [X]
Test result: DMT was not reactive toward RO_2• radicals in aqueous media.
Comments: The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.
Reference: Brown, S.L., *et al*., (1975).

B. **Test substance:** Dimethyl terephthalate
Test type: Hydrolytic half-life
Test method: Neutral water at 25^{o} C
GLP: Yes [ ]
No [X]
Test result: The half-life was 321-days
Comments: The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.

Reference: Mabey, W. and Mill, T. (1978) "Critical review of hydrolysis of organic compounds in water under environmental conditions" J. Phys. Chem. Ref. Data. 7(2):383-415. In "Health and Environmental Effects Profile for Dimethyl Terephthalate" (1984) EPA/600/X-84/152.

C. **Test substance:** Dimethyl terephthalate
Test type: Half-life
Test method:
GLP: Yes [ ]
No [X]
Test result: The half-life was estimated to be 1 to 4-weeks for surface water and 2 to 8-weeks for ground water.

Comments: The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.
Reference: Howard, P.H., *et al*., Page 464.

D. **Test substance:** Dimethyl terephthalate
Test type: Log sediment organic content/water partition coefficient
Test method: Calculated
GLP: Yes [ ]
No [X]
Test result: $K_{oc} = 2.49$
Comments: Information predates GLP regulations
Reference: Mabey, W.R., *et al*., (1984).

3.1.3 STABILITY IN SOIL

Test substance: Dimethyl terephthalate
Test type: Half-life
Test method:
GLP: Yes [ ]
No [X]
Test result: The half-life was estimated to be 1 to 4-weeks.
Comments: The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.
Reference: Howard, P.H., *et al*., Page 464.

3.2 MONITORING DATA (ENVIRONMENT)

3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

3.3.1 Distribution and Fugacity Calculation

Test type: Fugacity Modelling
Method: Level III Mackay-type, fugacity based models obtained from Trent University's Modeling Center. Specific model: Equilibrium Conctnration model (EQC) Level 3 model, version 1.01.
Remark: Default values were assumed for environmental compartment descriptions, dimensions, and properties, advective and dispersive properties. Chemical-specific parameters included Henry's Law Constant of 0.000134 atm*m^3/mol, vapor pressure of 0.01 mm Hg, melting point of 141 °C, log Kow of 2.25, and soil Koc of 72.9. These values were obtained by the model either through estimates or measured database values.
Distribution: Air (13.9%), Water (34.4%), Soil (51.6%), Sediment (0.134%).
Reliability: (2) valid with restrictions.
Source: Meylan, W. 2000. User's Guide for EPIWIN, Version 3.05.
Syracuse Research Corporation. North Syracuse, NY. March, 2000.

3.4 IDENTIFICATION OF MAIN MODE OF DEGRADABILITY IN ACTUAL USE

3.5 BIODEGRADATION

A. **Test substance:** Dimethyl terephthalate
Test type: Chemical oxygen demand (aerobic)
Test medium:
Test method:
GLP: Yes [ ]
No [X]
Test result: COD = 1.70 g oxygen/g
Comments: Information predates GLP regulations
Reference: Material and Safety Data Sheet; Eastman Chemical Company

B. **Test substance:** Dimethyl terephthalate
Test type: Bacterial degradation
Test medium: Activated sludge
Test method: Media was inoculated under aerobic conditions with 100 mg/l of DMT.
GLP: Yes [ ]
No [ ]
? [X]
Test result: Theoretical BOD = 84%
Comments: Japanese MITI test
Reference: Chemicals Inspection and Testing Institute (1992); Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan. Japan Chemical Industry Ecology – Toxicology and Information Center. ISBN 4-89074-101-1.

C. **Test substance:** Dimethyl terephthalate
Test type: Biological Degradation
Test medium: River water and Seawater
Test method: DMT at levels of 5, 40, and 50 ppm was cultivated for 3-days.
GLP: Yes [ ]
No [X]

Test result: Degradation rate was 100% in river water and 49, 38, and 27% in seawater at the low, medium and high dose levels.
Comments: None
Reference: Kondo, *et al*., (1988).

D. **Substance:** Dimethyl terephthalate
Test type: Bacterial degradation
Test medium: Mineral salts medium
Test method: 6000 ppm of test compound was incubated (shaken at 30^{o} C) with Pseudomonas acidovorans 256-1 for 40-days.
GLP: Yes [ ]
No [X]
Test result: No degradation was noted.
Comments: None
Reference: Kurane, R., *et al*., (1977).

E. **Test substance: Dimethyl terephthalate**
Test type: Bacterial degradation
Test medium:
Test method: DMT was incubated with a Rhodococcus species isolated from soil.
GLP: Yes [ ]
No [X]
Test result: The isolated bacterial species was capable of utilizing DMT as its sole carbon source completely degrading the molecule.

Comments: Similar results were obtained by Samsonova and Slizen using Rhodococcus erythropolis.
Reference: Ninnekar, H.Z., *et al*., (1985) and Slizen Z.M. (1989).

F. **Test substance: Dimethyl terephthalate**
Test type: Bacterial degradation
Test medium: Soil and wastewater containing DMT.
Test method: In one experiment, soil containing 100 mg DMT/400 g was inoculated with Rhodococcus erythropolis. In the second study, aerated wastewater from a DMT manufacturing facility was inoculated with 10% of a bacterial medium containing Rhodococcus erythropolis.
GLP: Yes [ ]
No [X]
Test result: DMT in soil was completely degraded after approximately 10-days. The inoculated wastewater degraded the DMT 100% after 212-hours.
Comments: None
Reference: Samsonova, A.S., *et al*., (1989).

G. **Test substance:** Dimethyl terephthalate
Test type: Bacterial degradation
Test medium:
Test method: DMT was incubated with Bacillus sp. isolated from garden soil.
GLP: Yes [ ]
No [X]

Test result: The isolated bacterial species was capable of utilizing DMT as its sole carbon source.
Comments: None
Reference: Sivamurthy, K., *et al*., (1989).

H. **Test substance:** Dimethyl terephthalate
Test type: Fungal degradation
Test medium:
Test method: Test compound was incubated with *Aspergillus niger* to assess its degradation potential.
GLP: Yes [ ]
No [X]
Test result: DMT was metabolized through monomethyl terephthalate, terephthalate, and protocatechuate with. Analysis of media using UV spectroscopy indicated 58% of the DMT was taken up in 144-hours.
Comments: None
Reference: Ganji, S.H., *et al.*, (1995).

I. **Test substance:** Dimethyl terephthalate
Test type: IC_{50}; Secondary waste water
Test medium:
Test method: 5-Hours
GLP: Yes [ ]
No [X]
Test result: IC_{50} = >5000 mg/L
Comments: Information predates GLP regulations
Reference: Material and Safety Data Sheet; Eastman Chemical Company

3.6 BOD, COD OR RATIO BOD/COD

3.7 BIOACCUMULATION

Test substance: Dimethyl terephthalate
Test type: Log bioconcentration factor (BCF)
Test method: Calculated by method of Kenaga (1980)
GLP: Yes [ ]
No [X]
Test result: BCF = 1.21
Comments: Information predates GLP regulations
Reference: In "Health and Environmental Effects Profile for Dimethyl Terephthalate" (1984) EPA/600/X-84/152.

4.1 ACUTE/PROLONGED TOXICITY TO FISH

A. **Test substance:** Dimethyl terephthalate
Test species: *Pimephales promelas* (Fathead minnow)
Test method: 96 hr, static
GLP: Yes [ ]
No [X]
Test results: LC_{50} = 9.6 mg/L, NOEC = 3 mg/kg
Comments: 30 mg/l was lethal to all fish
Reference: Eastman Kodak Co. 1984, unpublished data

B. **Test substance:** Dimethyl terephthalate
Test species: *Pimephales promelas* (Fathead minnow)
Test method: 96 hr, static
GLP: Yes [ ]
No [X]
Test results: LC_{50} = 45 mg/L
Comments: None
Reference: Eastman Kodak Co.1977, unpublished data

C. **Test substance:** Dimethyl terephthalate
Test species: *Pimephales promelas* (Fathead minnow)
Test method: 96 hr
GLP: Yes [ ]
No [ ]
? [X]
Test results: LC_{50} = 14.2 mg/L
Comments: None
Reference: Material Safety Data Sheet; DuPont Chemicals

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

A. **Test substance:** Dimethyl terephthalate
Test species: *Daphnia magna* (Water flea)
Test method: 96 hr, static
GLP: Yes [ ]
No [X]
Test results: LC_{50} = > 100 mg/L
Comments: None
Reference: Eastman Kodak Co. 1977, unpublished data

B. **Test substance:** Dimethyl terephthalate
Test species: *Daphnia magna* (Water flea)
Test method: 48 hr, static
GLP: Yes [ ]
No [X]
Test results: EC_{50} = >30 mg/L
Comments: Exposure to 30 mg/L induced 40% immobility
Reference: Eastman Kodak Co. 1984, unpublished data

C. **Test substance**: Dimethyl terephthalate
Test species: *Daphnia magna* (Water flea)
Test method: 48-hr
GLP: Yes [ ]
No [ ]
? [X]
Test results: LC_{50} = 30.4 mg/L
Comments: None
Reference: Material Safety Data Sheet; DuPont Chemicals

D. **Test substance:** Dimethyl terephthalate
Test species: *Dugesia tigrina* (Flatworm)
Test method: 96 hr, static
GLP: Yes [ ]
No [X]
Test results: LC_{50} = >100 mg/L
Comments: None
Reference: Eastman Kodak Co. 1977, unpublished data,

E. **Test substance:** Dimethyl terephthalate
Test species: *Helisoma trivolvis* (Snail)
Test method: 96 hr, static
GLP: Yes [ ]
No [X]
Test results: LC_{50} = >100 mg/L
Comments: None
Reference: Eastman Kodak Co. 1977, unpublished data

F. **Test substance:** Dimethyl terephthalate
Test species: *Helisoma trivolvis* (Snail)
Test method: 96 hr, static
GLP: Yes [ ]
No [X]
Test results: LC_{50} = >30 mg/L; NOEC 3 mg/L
Comments: None
Reference: Eastman Kodak Co. 1984, unpublished data

G. **Test substance:** Dimethyl terephthalate
Test species: *Gammarus fasciatus* (Sideswimmer)
Test method: 96 hr, static
GLP: Yes [ ]
No [X]
Test results: EC_{50} = >30 mg/L; NOEC 3 mg/L
Comments:
Reference: Eastman Kodak Co. 1984, unpublished data

4.3 TOXICITY TO AQUATIC PLANTS

A. **Test substance:** Dimethyl terephthalate; purity 99.99%
Test species: *Scenedesmus subspicatus* (algae)
Test method: Directive 88/302 EEC; 72-hr
GLP: Yes [X]
No [ ]

Test results:	Biomass	Growth Rate
	EC_{50}: 27.6 mg/L	EC_{50}: >32.3 mg/L
	EC_{10}: 14.3 mg/L	EC_{10}: 20.1 mg/L
	NOEC: 10.8 mg/L	NOEC: 10.8 mg/L

Comments: No analytical monitoring, concentrations were nominal. For the growth rate endpoint, an EC_{50} was not reached at the highest concentration tested (32.3 mg/L). At test beginning pH was 7.7-8.0 and it was 8.2-9.1 at conclusion. The estimated algal toxicity EC_{50} using ECOTOX software is 1.5 mg/L (96-hr).
Reference: Huls AG, unpublished data; Report AW-301; 1993

4.4 TOXICITY TO BACTERIA

Not available

4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS

Not available

4.5.1 CHRONIC TOXICITY TO FISH

Not available

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Not available

4.6 TOXICITY TO TERRESTRIAL ORGANISMS

4.6.1. TOXICITY TO SOIL DWELLING PLANTS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

A. **Test substance:** Dimethyl terephthalate

Test species: Ryegrass, Radish, Lettuce
Test method: 7-Day germination exposures to concentrations of 0, 1, 10, 100, or 1000 mg/L. There were 80 seeds used for each exposure test level and 40 seeds for control.
GLP: Yes [ ]
No [X]
Test results (No Adverse Effect Conc.): 10 mg/L (Rye grass, Radish), 1 mg/L (Lettuce)
Comments: Data predate GLP regulations
Reference: Eastman Kodak Co. 1976, unpublished data

B. **Test substance:** Dimethyl terephthalate

Test species: Ryegrass, Radish, Lettuce
Test method: Germination
GLP: Yes [ ]
No [X]
Test results (No Adverse Effect Conc.): 10 mg/L Rye grass, 30 mg/L (Radish, Lettuce)
Comments: Data predate GLP regulations; test duration and dose levels are unknown
Reference: Eastman Kodak Co. 1984, unpublished data

C. **Test substance:** Dimethyl terephthalate
Test species: Corn, Marigold, Lettuce, Radish
Test method: 1-week phytotoxicity to seedlings. Exposures to DMT concentrations of 0, 100, and 1000 mg/L. There were 10 corn seedlings and 20 seedlings for the other species per exposure level.
GLP: Yes [ ]
No [X]
Test results (No Adverse Effect Conc.): >1000 mg/L (Radish, Marigold, Lettuce), >100 mg/L, (Corn,)
Comments: Data predate GLP regulations
Reference: Eastman Kodak Co. 1976, unpublished data

D. **Test substance:** Dimethyl terephthalate
Test species: Corn, Marigold, Lettuce, Radish
Test method: Seedling growth
GLP: Yes [ ]
No [X]
Test results (No Adverse Effect Conc.): >10 mg/L (Radish), >33 mg/L (Lettuce, Corn, Marigold)
Comments: Data predate GLP regulations; test duration and dose levels are unknown
Reference: Eastman Kodak Co. 1984, unpublished data

E. **Test substance:** Wastewater from a DMT manufacturing facility
Test species: Jowar, Mung, Bajra
Test method: Plant germination effects were assessed using wastewater treated in the laboratory with a mixed culture of Pseudomonas sp., Aeromonas sp., Arthrobacter sp., and Bacillus sp.
GLP: Yes [ ]
No [ ]
? [X]
Test results (No Adverse Effect Conc.): The treated wastewater had no effect on germination rates in any species tested.
Comments: None
Reference: Goud, H.D., *et al*., (1990).

5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

A.	**Type:**	LD_0 []; LD_{100} []; LD_{50} [X]; LDL_0 []; Other []
	Species/strain:	Rat/Long-Evans Hooded
	Value:	>6,590 mg/Kg
	Method:	Oral doses of 0, 3000, 3900, 5020 or 6590 mg/Kg DMT were administered to groups of 3-6 male rats as a 20% solution in corn oil. The animals were observed for clinical signs of toxicity and mortality for 14-days. After 14-days of observations, the animals were euthanized, autopsied, and examined for gross pathology and histopathology.
	GLP:	Yes []; No [X]; ? []
	Test substance:	Commercial (Eastman Organic Chemicals)
	Remarks:	No mortality was observed during the 14-day post-treatment period. Clinical signs of toxicity were limited to slight to moderate weakness at all dose levels and slight tremors and ataxia at the 5,020 and 6,590 mg/Kg dose levels. No signs of gross or histopathological changes due to systemic toxicity were noted at necropsy.
	Reference:	Krasavage *et al*., 1973.
B.	**Type:**	LD_0 []; LD_{100} []; LD_{50} [X]; LDL_0 []; Other []
	Species/strain:	Rat
	Value:	4,390 mg/Kg
	Method:	Unknown
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT
	Remarks:	The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference.
	Reference:	Marhold, J.V., 1972.

5.1.2 ACUTE INHALATION TOXICITY

Type:	LC_0 []; LC_{100} []; LC_{50} [X]; LCL_0 []; Other []
Species/strain:	Rat
Value:	>6 mg/L
Method:	A two-hour inhalation exposure was conducted using a 100-liter chamber. DMT vapors (reported at 100-110°C; however, melting point is 142° C) were generated using a hot plate and introduced into the chamber containing six animals. Chamber temperature was between 25 and 29° C. Upon cooling, the vapors form a light, fluffy aerosol. Chamber concentrations were not reported. A control chamber was used but not described.
GLP:	Yes []; No [X]; ? []
Test substance:	DMT

Remarks:	Respiratory irritation was evident along with mucosal hyperemia, increased excitation upon stimulation, irregular breathing, and cyanosis in animals exposed to the hot vapor. No deaths were reported. Interpretation of the study is limited by the lack of detail in the study report.
Reference:	Sanina, Y.P. and Kochetkova, T.A., 1963.

5.1.3 ACUTE DERMAL TOXICITY

Type:	LD_0 []; LD_{100} []; LD_{50} [X]; LDL_0 []; Other []
Species/strain:	Guinea Pig
Value:	>5,000 mg/Kg
Method:	Unknown
GLP:	Yes []; No [X]; ? []
Test substance:	DMT
Remarks:	The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference.
Reference:	Patty's Industrial Hygiene and Toxicology, 3rd Revised Edition, 1981.

5.2 CORROSIVENESS/IRRITATION

5.2.1 SKIN IRRITATION/CORROSION

A.	**Species/strain:**	Guinea Pig
	Results:	Highly corrosive []; Corrosive []; Highly irritating []; Moderately irritating []; Slightly irritating [X]; Not irritating []
	Method:	DMT was moistened with water and applied (1 and 2 g/Kg) to two animals using gauze. It was held in place with a rubber cuff for 24-hours.
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT
	Remarks:	Slight redness, no edema
	Reference:	Unpublished data, Eastman Kodak Co., (1957).
B.	**Species/strain:**	Guinea Pig
	Results:	Highly corrosive []; Corrosive []; Highly irritating []; Moderately irritating [X]; Slightly irritating []; Not irritating []
	Method:	Solid DMT was moistened with water and applied (0.25 – 1.0 g/Kg) to three animals using a gauze. It was held in place with a rubber cuff for 24-hours.
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT
	Remarks:	Erythema and slight to moderate edema were noted with sparse hair at 2-weeks.
	Reference:	Unpublished data, Eastman Kodak Co., (1963).

C.	**Species/strain:**	Mouse
	Results:	Highly corrosive []; Corrosive []; Highly irritating []; Moderately irritating []; Slightly irritating [X]; Not irritating []
	Method:	The tails of mice were inserted into test tubes containing a suspension of DMT (conc. not reported) in 5% starch for 2-hours/day for 10-days.
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT
	Remarks:	Repeated submersion of the tails induced a transient (1-2 hr duration) slight hyperemia after the third exposure. Behavioral changes were noted after 6 submersions. Tails and behavior were reported to be normal by Day 12. Interpretation of the study is limited by the lack of detail in the study report.
	Reference:	Sanina, Y.P. and Kocketkova, T.A., 1963.
D.	**Species/strain:**	Rabbit
	Results:	Highly corrosive []; Corrosive []; Highly irritating []; Moderately irritating []; Slightly irritating [X]; Not irritating []
	Method:	The skin of rabbits (free of fur) were exposed to a suspension of DMT (conc. not reported) in 5% starch for 2-hours, after which the test material was washed away with warm water. Up to 10 applications were performed.
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT
	Remarks:	Repeated application to the skin induced a slight irritation after 3-days that was reported to have disappeared on Day 4. A pigmentation was noted after 10 applications. The skin was reported to be normal by Day 12. Interpretation of the study is limited by the lack of detail in the study report.
	Reference:	Sanina, Y.P. and Kocketkova, T.A., 1963.

5.2.2 EYE IRRITATION/CORROSION

A.	**Species/strain:**	Rabbit
	Results:	Highly corrosive []; Corrosive []; Highly irritating []; Moderately irritating []; Slightly irritating []; Not irritating [X]
	Method:	Unknown
	GLP:	Yes []; No [X]; ?[ ]
	Test substance:	DMT
	Remarks:	No damage or irritation was noted
	Reference:	Unpublished data, Eastman Kodak Co., (1957).
B.	**Species/strain:**	Rabbit
	Results:	Highly corrosive []; Corrosive []; Highly irritating []; Moderately irritating []; Slightly irritating [X]; Not irritating []

	Method:	500 mg of DMT was placed in the eyes for 24-hours.
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT
	Remarks:	The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.
	Reference:	Anonymous, 1986; RTECS 1988.
C.	**Species/strain:**	Unknown
	Results:	Highly corrosive []; Corrosive []; Highly irritating []; Moderately irritating []; Slightly irritating [X]; Not irritating []
	Method:	Unknown
	GLP:	Yes []; No [X]; ? [ ]
	Test substance:	DMT
	Remarks:	A pronounced irritating effect on the mucous membranes of the eyes was induced. The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.
	Reference:	Kamal' Dinova, Z. M., *et al*., 1962.
D.	**Species/strain:**	Rabbit
	Results:	Highly corrosive []; Corrosive []; Highly irritating []; Moderately irritating []; Slightly irritating [X]; Not irritating []
	Method:	Two drops of DMT suspended in a starch solution were instilled.
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT
	Remarks:	Interpretation of the study is limited by the lack of detail in the study report.
	Reference:	Sanina, Y.P. and Kochetkova, T.A., 1963.
E.	**Species/strain:**	Rabbit
	Results:	Highly corrosive []; Corrosive []; Highly irritating []; Moderately irritating []; Slightly irritating [X]; Not irritating []
	Method:	Unknown
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT
	Remarks:	The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.
	Reference:	Patty's Industrial Hygiene and Toxicology, 2nd Edition, 1963.

5.3 SKIN SENSITIZATION

A.	**Type:**	"Drop-on"
	Species/strain:	Guinea Pig

	Results:	Sensitizing []; Not Sensitizing [X]; Ambiguous []
	Method:	A drop-on skin sensitization study was conducted with 0.5 ml of a 1% solution of DMT in acetone:dioxane:guinea pig fat (7:2:1) dropped onto the rump area of 10 animals. Primary irritation was determined at 24 and 48-hours post-dosing. Three additional dose applications occurred over the next five-days and then the animals remained unexposed for 3-weeks. Challenge doses were applied to the right and left shoulders the next two-weeks, respectively. Erythema and edema were scored on a scale of 0 to 4.
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT (Eastman Organic Chemicals).
	Remarks:	Neither primary irritation nor skin sensitization was induced by DMT.
	Reference:	Krasavage, W.J. *et al*., 1973.
B.	**Type:**	"Footpad"
	Species/strain:	Guinea Pig
	Results:	Sensitizing []; Not Sensitizing [X]; Ambiguous []
	Method:	0.5 ml of a 1% solution of DMT in acetone:dioxane:guinea pig fat (7:2:1) dropped onto the rump area of 10 animals. Primary irritation was determined at 24 and 48-hours post-dosing. After one-week, a mixture of the dosing compound (a 1% solution of DMT in acetone:dioxane:guinea pig fat (7:2:1) was mixed with whole heparinized rabbit blood (1%) for 1 to 3-hours and 0.05 ml injected into the footpad of the animals. A challenge dose (0.5 ml of a 1% solution of DMT in acetone:dioxane:guinea pig fat (7:2:1) was administered by drop-on one-week later. Sensitization scores were recorded at 24 and 48-hours after the challenge dose.
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT (Eastman Organic Chemicals).
	Remarks:	Neither primary irritation nor skin sensitization was induced by DMT.
	Reference:	Krasavage, W.J., *et al*., 1973.
C.	**Type:**	Unknown
	Species/strain:	Guinea Pig
	Results:	Sensitizing []; Not Sensitizing [X]; Ambiguous []
	Method:	Animals received 5,000 mg/kg dermal exposure of DMT.
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT (Eastman Organic Chemicals).
	Remarks:	DMT induced slight irritation but no sensitization reaction. The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.
	Reference:	Patty's Industrial Hygiene and Toxicology, 3rd Revised Edition, 1981.

5.4 REPEATED DOSE TOXICITY

A.	**Species/strain:**	Rat
	Sex:	Unknown
	Route of administration:	Oral, gavage
	Exposure period:	14-Days
	Frequency of treatment:	5-Days/week
	Post-exposure observation period:	At least 11-days (Actual length is not noted)
	Dose:	5,000 mg/kg/day
	Control group:	Yes []; No []; No data [X]; Concurrent no treatment []; Concurrent vehicle []; Historical []
	NOEL:	Not determined
	LOEL:	5,000 mg/kg/day
	Results:	While no rats died during the 10-day exposure dosing period, 5 of 6 animals died with pathology indicative of starvation by Day 11 after exposure had ended. During the exposure period, animals exhibited transient signs of discomfort and progressive weight loss. There was no hematuria or polyuria, nor was there any crystalline precipitates observed in the urine. There were no calculi or crystals in the bladder or kidneys of the rats at necropsy.
	Method:	Rats were administered DMT for 10-days in a two-week period.
	GLP:	Yes []; No []; ? [X]
	Test substance:	DMT
	Remarks:	Interpretation of the study is limited by the lack of detail in the report.
	Reference:	Haskell Laboratory, Du Pont Co., unpublished data, MR-423-1.
B.	**Species/strain:**	Rat (weanling)/F-344
	Sex:	Male and Female
	Route of administration:	Oral, feed
	Exposure period:	14-Days
	Frequency of treatment:	7-Days/week
	Post-exposure observation period:	None
	Dose:	0, 0.5, 1.0, 1.5, 2, or 3% (females: 638, 1277, 1790, 2290, and 3020 mg/kg; males: 660, 1320, 1890, 2260, and 2590 mg/kg) DMT
	Control group:	Yes [X]; No []; No data []; Concurrent no treatment [X]; Concurrent vehicle []; Historical []
	NOEL:	0.5% (660 mg/kg) (males); 1.0% (1277 mg/kg) (females)
	LOEL:	-
	Results:	Average BW of the animals consuming the 1.5% and above was decreased on study Days 6-8 and

12-14 (postnatal Days 34-36 and 40-42) in females and 1.0% in males. Decreases in BW were accompanied by reduced feed consumption (possible palatability problems). There was no effect on water consumption at any dose. The incidence of bladder calculi in males from the 0, 0.5, 1.0, 1.5, 2.0, and 3.0% DMT dietary groups were 0, 0, 0, 35, 72, and 100%, respectively. The incidence of bladder calculi in females from the 0, 0.5, 1.0, 1.5, 2.0, and 3.0% DMT dietary groups were 0, 0, 0, 0, 36, and 47%, respectively. Grossly observable irregular thickening of the bladder wall was limited to animals having bladder calculi. The composition of the bladder calculi from the DMT treated animals was primarily calcium and terephthalic acid (TPA) with 5-7% protein. Phosphate levels were low, in contrast to bladder calculi from animals treated directly with terephthalic acid. Neither oxalate, nor uric acid, was found in the calculi. An acidic urinary pH was believed to have induced the hypercalciuria, a characteristic of urolithiasis in man. The higher urinary concentrations of TPA from DMT in the diet (when compared to similar dietary concentrations of TPA) explained the higher incidence of urinary calculi from the DMT diets than from comparable levels of TPA in the diet. Urinary phosphate levels were decreased in the animals consuming the DMT diet and explained why phosphate was present only at very low levels in the bladder calculi in those animals.

Method: Rats (13-18/sex/dose group) were fed DMT diets for a period of two-weeks. Individual body weights and total feed and water intake per cage were collected. At necropsy, urine was collected directly from the bladder for pH measurement, and concentrations of "stone-forming" materials were determined. The urinary system was examined grossly for presence of macroscopic calculi. Any calculi were collected, dried, weighed and analyzed. This study also evaluated terephthalic acid (TPA) at similar dietary levels.

GLP: Yes []; No []; ? [X]

Test substance: DMT (Eastman Chemical, Lot No. A9A), ground and filtered through a No. 35 sieve**.**

Remarks: Weanling rats are probably more sensitive to the induction of bladder calculi than adults due to their very high feed consumption rates relative to body weight.

	Reference:	Chin, T.Y. *et al*., 1981.
C.	**Species/strain:**	Rat
	Sex:	Unknown
	Route of administration:	Oral, feed
	Exposure period:	5% (16-Days); 10% (>16-Days)
	Frequency of treatment:	7-Days/week
	Post-exposure observation period:	None
	Dose:	5 and 10%
	Control group:	Yes []; No []; No data [X]; Concurrent no treatment []; Concurrent vehicle []; Historical []
	NOEL:	Not determined
	LOEL:	5%
	Results:	Hematuria was observed in all rats at some time during the study. All rats from the group consuming a diet containing 5% DMT and killed on Day 17 had bladder stones and 3 of 5 had minute calculi in their kidneys. Four of six rats consuming the 10% DMT diet died between study Days 2 and 17. With the exception of one rat that died on Day 2, all animals consuming the 10% DMT diet exhibited hematuria and had urinary bladder or kidney stones.
	Method:	Rats were fed DMT in their diets at a rate of 5 and 10%. The 5% dose group was sacrificed after 16-days.
	GLP:	Yes []; No []; ? [X]
	Test substance:	DMT
	Remarks:	Interpretation of the study is limited by the lack of detail in the report.
	Reference:	Haskell Laboratory, Du Pont Co., unpublished data, MR-423-1.
D.	**Species/strain:**	Rat
	Sex:	Males
	Route of administration:	Oral, feed
	Exposure period:	28-Days
	Frequency of treatment:	7-Days/week
	Post-exposure observation period:	None
	Dose:	5% DMT in diet; 3,750 mg/kg/day
	Control group:	Yes [X]; No []; No data []; Concurrent no treatment [X]; Concurrent vehicle []; Historical []
	NOEL:	Not determined
	LOEL:	5%
	Results:	DMT animals consumed approx. half the amount of feed as controls and lost approx. 40 grams over the 28-day period, while controls gained approx. 135 grams. One DMT animal died on Day 16. At no time point did hematological parameters show

		any abnormalities. Also histopathological examination of selected tissues did not reveal any lesions attributable to DMT exposure. After 28-days on test diet the four remaining animals were returned to the control diet. Interestingly, these four animals died the first night upon return to the control diet.
	Method:	Diets containing DMT were fed to rats (5/dose) for 28-days. Body weights and feed consumption were recorded and hematological parameters were collected at the beginning, middle and end of the feeding period.
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT
	Remarks:	Interpretation of the study is limited by the lack of detail in the report.
	Reference:	Patty's Industrial Hygiene and Toxicology, 3rd Edition, 1981.
E.	**Species/strain:**	Rat
	Sex:	Unknown
	Route of administration:	Oral, feed
	Exposure period:	35 to 39-Days (500 mg/kg) and longer for the lower dose levels
	Frequency of treatment:	7-Days/week
	Post-exposure observation period:	None
	Dose:	0.5, 7.5, and 500 mg/kg/day
	Control group:	Yes [X]; No []; No data []; Concurrent no treatment [X]; Concurrent vehicle []; Historical []
	NOEL:	500 mg/kg/day
	LOEL:	-
	Results:	Rats exposed to 500 mg/kg/day for 35 to 39-days or 0.5 and 7.5 mg/kg/day for a longer duration did not differ from control animals.
	Method:	Animals were administered DMT in their diets for various time periods.
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT
	Remarks:	The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.
	Reference:	Prusakov, V.M., 1966.
F.	**Species/strain:**	Rat
	Sex:	Male and Female
	Route of administration:	Oral, feed
	Exposure period:	13-Weeks
	Frequency of treatment:	7-Days/week

	Post-exposure observation period:	None
	Dose:	0.5, 1.6 or 3% DMT in diet
	Control group:	Yes []; No []; No data [X]; Concurrent no treatment []; Concurrent vehicle []; Historical []
	NOEL:	Not determined
	LOEL:	0.5%
	Results:	The incidence of bladder calculi in animals fed diets containing 3% DMT for 13-weeks was 12/16 and 6/16 in male and female rats, respectively. The incidence of bladder calculi in male rats fed diets containing 1.6% DMT was 1/19, and 2/19 in the 0.5% exposure group. Calculi were not noted in mid- and low-dose females. The incidence of moderate hyperplasia of the internal bladder epithelial lining in animals fed diets containing 3% DMT for 13-weeks was 11/16 and 7/16 in males and females, respectively. Of the animals fed the 3% DMT diet and developing hyperplasia of the bladder lining, calculi were found in 11/11 males and 6/7 females. There were no neoplastic changes.
	Method:	Rats (7-19/group) were fed DMT diets for 13-weeks.
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT
	Reference:	Vogin, E. E., 1972.
G.	**Species/strain:**	Rat and Mouse
	Sex:	Male and Female
	Route of administration:	Oral, feed
	Exposure period:	13-Weeks.
	Frequency of treatment:	7-Days/week
	Post-exposure observation period:	None
	Dose:	1750, 2500, 5000, 10000 or 20000 ppm
	Control group:	Yes [X]; No []; No data []; Concurrent no treatment [X]; Concurrent vehicle []; Historical []
	NOEL:	Rat 5000 ppm (NOAEL), Mouse 20000 ppm (NOAEL)
	LOEL:	-
	Results:	No compound-related effects were noted in the physical appearance, behavior, or feed consumption measures of either species. No deaths occurred in the rats. One male mouse at 2500, 5000, and 20000 ppm died during the study, and two females at 20000 ppm. Body weight gains of males fed 20000 ppm was 83% of controls. Body weight gains of females fed 10000 and 20000 ppm was 83% and 71% of their respective controls.

		There were no differences in body weight or body weight gain in the male and female mice receiving DMT in the diet. No gross lesions were observed in rats or mice at necropsy. Microscopic examinations of the livers from both species in all dose groups revealed diffuse hepatocellular swelling. Although this change was considered compound related, it was not manifested in a dose-related manner.
	Method:	Groups (10/sex) of rats and mice were fed DMT in their diets for 13-weeks. Physical appearance and behavior were noted and feed consumption and body weights were measured.
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT
	Reference:	National Cancer Institute Technical Report Series, NCI-CG-TR-121, No. 121, 1979.
H.	**Species/strain:**	Rat/Long-Evans Hooded
	Sex:	Males
	Route of administration:	Oral, feed
	Exposure period:	96-Days
	Frequency of treatment:	7-Days/week
	Post-exposure observation period:	Till natural death
	Dose:	0, 0.25, 0.5 and 1.0% (152, 313, 636 mg/kg)
	Control group:	Yes [X]; No []; No data []; Concurrent no treatment [X]; Concurrent vehicle []; Historical []
	NOEL:	0.5% (313 mg/kg)
	LOEL:	-
	Results:	The only toxicological effect seen in the study was a reduced weight gain in the high dose animals. No toxicological effects on hematocrit, hemoglobin, white blood cell or differential counts were seen in any group. No dose-related changes were seen in BUN, SGOT, OCT, SAP, blood glucose, or serum protein values. Average body and relative and absolute liver and kidney weights of the experimental groups did not differ significantly from control weights. Microscopic examination of tissues from all organ systems revealed no morphologic evidence of any abnormalities that could be attributed to compound exposure.
	Method:	Weanling rats (30/group) were exposed to DMT in a basal diet. Ten animals from each group were sacrificed after 96-days, and tissue samples from

		all major organ systems were removed for histologic examination. Livers and kidneys were weighed for organ weight comparisons. Hematology and serum biochemistry's were conducted on Days 55 and 90. The remaining animals were placed back onto control diet for observation of potential long-term effects over the rest of their life.
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT (Eastman Organic Chemicals, Cat. No. 6580).
	Reference:	Krasavage, W.J., *et al*., 1973.
I.	**Species/strain:**	Rat
	Sex:	Unknown
	Route of administration:	Inhalation
	Exposure period:	5-Months
	Frequency of treatment:	2-Hours/day
	Post-exposure observation period:	None
	Dose:	1-4 or 40-70 mg/m^3
	Control group:	Yes []; No []; No data [X]; Concurrent no treatment []; Concurrent vehicle []; Historical []
	NOEL:	Not determined
	LOEL:	1-4 mg/m^3
	Results:	At 1-4 mg/m^3, conjunctivitis, hypoactivity, a decrease in blood pressure, erythrocytopenia, reticulocytosis, leukopenia, and an increased electrical neuro-excitability was noted. At 40-70 mg/m^3, 30% mortality, rhinitis, depilation, dystrophic changes in the liver and kidneys, hemorrhage of the lungs, brain and myocardium, and hyperemia of the internal organs were reported.
	Method:	Inhalation exposure for five-months.
	GLP:	Yes []; No [X]; ?[]
	Test substance:	DMT
	Remarks:	Interpretation of the study is limited by the lack of detail in the study report.
	Reference:	Sanina, Y.P. and Kocketkova, T.A., 1963.
J.	**Species/strain:**	Rat/Long-Evans Hooded
	Sex:	Male
	Route of administration:	Inhalation
	Exposure period:	3-Months (58 exposure)
	Frequency of treatment:	4-Hours/day, 5-Days/week
	Post-exposure observation period:	Till natural death
	Dose:	0.0, 16.5, and 86.4 mg/m^3
	Control group:	Yes [X]; No []; No data []; Concurrent no treatment [X]; Concurrent vehicle [];

		Historical []
	NOEL:	16.5 mg/m^3
	LOEL:	-
	Results:	Nose rubbing, preening and blinking were noted soon after the start of DMT exposures of 86.4 mg/m^3. These symptoms continued intermittently throughout the exposure period and were repeated during succeeding exposures, but were not seen at the lower concentration. No toxicological effects on hematocrit, hemoglobin, white blood cell or differential counts were seen in any of the treated groups. No dose-related changes were seen in BUN, SGOT, OCT, SAP, blood glucose or serum protein values. Average body and relative and absolute liver and kidney weights of the treated animals sacrificed at study termination did not differ significantly from control weights. Microscopic examination of tissues from all organ systems examined revealed no morphologic evidence of abnormalities attributable to DMT exposure.
	Method:	Groups of rats (30/dose) were exposed to DMT "dust clouds" containing 0.0, 16.5, and 86.4 mg/m^3 for 4-hours per day for 58 exposures (excluding weekends and holidays) over a 3-month period using one cubic meter inhalation chambers (University of Rochester type). The in-chamber temperature was 24-26^o C. The dust-cloud of DMT entered the chamber from the top via the air supply stream and was exhausted from the bottom. Within 24-hours after the last exposure, 10 rats were sacrificed, and tissue samples from all major organ systems were processed for histologic examination. Hematology and serum biochemistry's were conducted on approximately Days 55 and 90. Livers and kidneys were weighted for organ weight comparisons. The remaining animals (20/group) were put on the control diet and were observed for long-term effects over the remainder of their life.
	GLP:	Yes []; No [X]; ? []
	Test substance:	DMT (Eastman Organic Chemicals, Cat No.6580).
	Reference:	Krasavage, W.J., *et al.*, 1973.
K.	**Species/strain:**	Rat and Guinea Pig
	Sex:	Unknown
	Route of administration:	Inhalation
	Exposure period:	6-Months.
	Frequency of treatment:	6-Hours/day, 5-Days/week
	Post-exposure observation period:	None

	Dose:	15 mg/m^3 (The amount of respirable DMT was only 5 mg/m^3)
	Control group:	Yes []; No []; No data [X]; Concurrent no treatment []; Concurrent vehicle []; Historical []
	NOEL:	15 mg/m^3 (NOEL).
	LOEL:	-
	Results:	There were no detectable effects on body weights, or routine clinical chemistry or urinalysis parameters. Gross and histopathological evaluations of tissues from these animals were within normal limits.
	Method:	Inhalation - Exposure 6-hours a day, 5-days a week, for 6-months to 15 mg/m^3 of DMT. The amount of respirable DMT was only 5 mg/m^3.
	GLP:	Yes []; No []; ? [X]
	Test substance:	DMT
	Remarks:	The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.
	Reference:	Lewis, T.R. *et al*., 1982.
L.	**Species/strain:**	Rat
	Sex:	Unknown
	Route of administration:	Inhalation
	Exposure period:	"Chronic"
	Frequency of treatment:	Unknown
	Post-exposure observation period:	None
	Dose:	0.08, 0.4 or 1 mg/m^3
	Control group:	Yes []; No []; No data []; Concurrent no treatment []; Concurrent vehicle []; Historical []
	NOEL:	Not determined
	LOEL:	0.08 mg/m^3
	Results:	Exposure to 1 mg/m^3 caused a substantial increase in basal and dopamine-inducible activity of adenylate cyclase. No note-worthy change was seen after exposure to 0.08 or 0.4 mg/m^3. Exposure to DMT also induced a dose-dependent inhibition of phosphodiesterase. Acetylcholinesterase activity was also inhibited in the synaptosomal-mitochondrial fraction of the brain cortex, but no effect was noted in its activity in the microsomal membrane.
	Method:	Chronic inhalation exposure to 0.08, 0.4 or 1 mg/m^3 of DMT.
	GLP:	Yes []; No []; ? [X]
	Test substance:	DMT
	Remarks:	The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the

		primary reference, and is limited by the lack of detail in the report.
	Reference:	Davidenko, A.V. *et al*., 1982.
M.	**Species/strain:**	Rat
	Sex:	Unknown
	Route of administration:	Inhalation
	Exposure period:	"Chronic"
	Frequency of treatment:	Unknown
	Post-exposure observation period:	None
	Dose:	0.08, 0.4 or 1 mg/m^3
	Control group:	Yes []; No []; No data [X]; Concurrent no treatment []; Concurrent vehicle []; Historical []
	NOEL:	Not determined.
	LOEL:	0.08 mg/m^3
	Results:	The chronic effect of DMT on rats induced a significant decrease in the uptake of radiolabeled noradrenaline by gray matter synaptosomes. At 0.4 mg/m^3, uptake was decreased 20%, while at 1 mg/m^3, the decrease was 51%. No effect was noted on monoamine oxidase or catecholamine-o-methyl transferase activities.
	Method:	Inhalation exposure to 0.08, 0.4 or 1 mg/m^3 of DMT
	GLP:	Yes []; No []; ? [X]
	Test substance:	DMT
	Remarks:	The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.
	Reference:	Davidenko, A.V. *et al*., 1984.
N.	**Species/strain:**	Rat
	Sex:	Unknown
	Route of administration:	Subcutaneous
	Exposure period:	10-Days and 2.5-Months
	Frequency of treatment:	Once/day
	Post-exposure observation period:	None
	Dose:	10-Days at 2 g/kg (for 10-days) and for 1 g/kg (for 2.5-months)
	Control group:	Yes []; No []; No data [X]; Concurrent no treatment []; Concurrent vehicle []; Historical []
	NOEL:	2 g/kg for 10-days. Not determined for the 2.5-month period.
	LOEL:	-
	Results:	No significant effects were noted in any of the assessed parameters following 10-days of exposure to 2 g/kg of DMT. The only observation noted

	following a 2.5-month exposure period was reduced body weight gain.
Method:	Subcutaneous injection of DMT in 20% oil emulsions. Information on body weight, organ vitamin C content, hematology, serum protein, and cholinesterase activity were assessed.
GLP:	Yes []; No [X]; ? []
Test substance:	DMT
Remarks:	Interpretation of the study is limited by the lack of detail in the study report.
Reference:	Slyusar, M.P. and Cherkasov, I.A., 1964.

5.5 GENETIC TOXICITY IN VITRO

A. BACTERIAL TEST

A -	**Type**:	Bacterial reverse mutation assay
	System of testing:	Species/strain: *Salmonella typhimurium* TA98, TA100, TA1535, and TA1537
	Concentration:	3.3 to 333 µg/plate
	Metabolic activation:	With []; Without []; With and Without [X]; No data []
	Results:	
	Cytotoxicity conc.:	With metab. activation: 666 ug Without metab. activ.: 666 ug
	Precipitation conc.:	Not determined
	Genotoxic effects:	+ ? - With metab. activation: [] [] [X] Without metab. activ.: [] [] [X]
	Method:	Modified Ames *et al.*, (1975)
	GLP:	Yes []; No []; ? [X]
	Test Substance:	DMT (Aldrich; purity 99%)
	Remarks:	Procedure: Pre-incubation Plates/test: Unknown Activation system: S-9 was from Aroclor 1254-induced male SD rats and Syrian hamsters. Media: Histidine selective Number of replicates: 2
	Reference:	Zeiger, E., *et al.*, 1982. Zeiger, E., *et al.*, 1985.
B -	**Type:**	Bacterial reverse mutation assay
	System of testing:	Species/strain: *Salmonella typhimurium* TA98, TA100.
	Concentration:	Unknown
	Metabolic activation:	With []; Without []; With and Without [X]; No data []
	Results:	
	Cytotoxicity conc.:	With metab. activation: Unknown Without metab. activ.: Unknown

Precipitation conc.: Not determined

Genotoxic effects:

	+	?	-
With metab. activation:	[]	[]	[X]
Without metab. activ.:	[]	[]	[X]

Method: The standard Ames assay with major modifications (shifting of histidine and biotin from the top to the bottom agar and reducing the glucose concentration to 67.5 mg/plate in the bottom agar).

GLP: Yes []; No []; ? [X]

Test Substance: DMT

Remarks: Procedure: Unknown
Plates/test: Unknown
Activation system: S-9 was from Aroclor 1254-induced male SD rats
Media: Histidine selective
Number of replicates: Unknown

Reference: Kozumbo, W.J., *et al.*, 1982.

C - Type: Bacterial reverse mutation assay

System of testing: Species/strain: *Salmonella typhimurium* TA98, TA100, TA102, TA1535, TA1537, and TA1538

Concentration: 0.5 - 5,000 µg/plate

Metabolic activation: With []; Without []; With and Without [X]; No data []

Results:

Cytotoxicity conc.: With metab. activation: 5,000 ug
Without metab. activ.: 5,000 ug

Precipitation conc.: Unknown

Genotoxic effects:

	+	?	-
With metab. activation:	[]	[]	[X]
Without metab. activ.:	[]	[]	[X]

Method: Ames *et al.*, (1975) with DMT dissolved in a mixture of DMSO and Tween 20 (29:1).

GLP: Yes []; No []; ? [X]

Test Substance: DMT (Italian PET plastic industry, purity not reported).

Remarks: Procedure: Unknown
Plates/test: Unknown
Activation system: S-9
Media: Unknown
No. replicates: Unknown

Reference: Monarca, S., *et al.*, 1991.
Monarca, S., *et al.*, 1989.

D - Type: Bacterial reverse mutation assay

System of testing: Species/strain: *Photobacterium phosphorium*

Concentration: Unknown

Metabolic activation: With []; Without [X]; With and Without []; No data []

Results:

Cytotoxicity conc.: With metab. activation: Unknown

Without metab. activ.: Unknown

Precipitation conc.: Unknown

Genotoxic effects:

	+	?	-
With metab. activation:	[]	[]	[]
Without metab. activ.:	[]	[X]	[]

Method: Mutatox™ Assay; This assay utilizes dark mutants that have lost the ability to produce light via repression of the operon responsible for luminescence. Luminescence can be restored (derepressed) via several mechanisms such as direct interaction with the repressor region or interference with synthesis of the repressor.

GLP: Yes []; No []; ? [X]

Test Substance: DMT (Aldrich; purity 99%)

Remarks: Procedure: Unknown
Plates/test: Unknown
Activation system: None
Media: Unknown
No. replicates: Unknown

Reference: Elmore, E. and Fitzgerald, M.P., 1990.

B. NON-BACTERIAL IN VITRO TEST

A - Type: DNA single-strand breaks

System of testing: Species/strain: Rat hepatocytes

Concentration: 0, 3.75, 7.50, or 15.00 µmole/ml equivalent to 0, 727.5, 1,455, or 2,910 µg/ml

Metabolic activation: With [X]; Without []; With and Without []; No data []

Results:

Cytotoxicity conc.: With metab. activ.: >2,910 µg/ml
Without metab. activation: NA

Precipitation conc.:

Genotoxic effects:

	+	?	-
With metab. activ.:	[]	[]	[X]
Without metab. activ.:	[]	[]	[]

Method: DMT was dissolved in a mixture of DMSO and Tween 20 (29:1). Rat hepatocytes were isolated by conventional methods. Cytotoxicity (trypan blue exclusion) was measured following a 1-hour incubation period. The remaining cells were lysed and DNA was isolated on filters and eluted at alkaline pH. DNA was measured in the eluted fractions by fluorometric determinations using a Hoechst 33258 dye. A positive finding is designated when the percent DNA retained on the control filter minus the percent DNA retained on the filters from each treatment group is greater than 20% at dose levels with greater than 70% viability.

GLP: Yes []; No []; ? [X]

	Test Substance:	DMT (Italian PET plastic industry, purity not reported)
	Remarks:	Procedure: Primary rat hepatocytes were used Plates/test: Unknown Activation system: Primary rat hepatocytes Media: Unknown No. replicates: Unknown
	Reference:	Monarca, S., *et al.*, 1991. Monarca, S., *et al.*, 1989.
B -	**Type:**	DNA single-strand breaks
	System of testing:	Species/strain: SV40-transformed Chinese Hamster Embryo cell line (CO60 cells)
	Concentration:	0, 3.75, 7.50, or 15.00 µmole/ml equivalent to 0, 727.5, 1,455, or 2,910 µg/ml.
	Metabolic activation:	With []; Without [X]; With and Without []; No data []
	Results:	
	Cytotoxicity conc.:	With metab. activation: NA Without metab. activ.: >2,910 µg/ml
	Precipitation conc.:	Unknown
	Genotoxic effects:	+ ? - With metab. activ.: [] [] [] Without metab. activ.: [] [] [X]
	Method:	DMT was dissolved in a mixture of DMSO and Tween 20 (29:1). Cytotoxicity (trypan blue exclusion) was measured following a 1-hour incubation period. Cells were lysed and DNA was isolated on filters and eluted at alkaline pH. DNA was measured in the eluted fractions by fluorometric determinations using a Hoechst 33258 dye. A positive finding is designated when the percent DNA retained on the control filter minus the percent DNA retained on the filters from each treatment group is greater than 20% at dose levels with greater than 70% viability.
	GLP:	Yes []; No []; ? [X]
	Test Substance:	DMT (Italian PET plastic industry, purity not reported)
	Remarks:	Procedure: SV40-transformed Chinese Hamster Embryo cell line (CO60 cells). Plates/test: Unknown Activation system: None Media: Unknown No. replicates: Unknown Other: Results of this test were not fully reported.
	Reference:	Monarca, S., *et al.*, 1991. Monarca, S., *et al.*, 1989.

C - Type: Unscheduled DNA synthesis
System of testing: Species/strain: Human/Hela
Concentration: 5, 50, 500, 5,000 µg/ml
Metabolic activation: With []; Without []; With and Without [x]; No data []

Results:
Cytotoxicity conc.: With metab. activation: Unknown
Without metab. activ.: Unknown

Precipitation conc.: Unknown
Genotoxic effects:

	+	?	-
With metab. activ.:	[]	[]	[X]
Without metab. activ.:	[]	[]	[X]

Method: Induction of unscheduled DNA synthesis was measured in HeLa cells exposed to varying concentrations of DMT dissolved in a mixture of DMSO and Tween 20 (29:1). DMT exposures were conducted in PBS with or without S9 liver fractions. Following treatment and rinsing to remove residual material, the cells were incubated with or without hydroxyurea (HU) in culture media. Tritiated methylthymidine was added after 15 minutes and the incubations continued for three-hours. Radioactivity was then counted to determine the incorporation of the radiolabeled thymidine. Inhibition of DNA replication and synthesis by HU in the control and treated cultures was determined by comparing the ratio of counts from 1) control w/o HU ÷ control plus HU, and 2) treated w/o HU ÷ treated plus HU. Inhibition of DNA replication and synthesis by DMT exposure was determined by the ratio of treated w/o HU ÷ control w/o HU. The effect of HU on the induction of DNA repair in the presence of DMT was determined by the ratio of (treated plus HU ÷ treated w/o HU) divided by (control plus HU ÷ control w/o HU).

GLP: Yes []; No []; ? [X]
Test Substance: DMT (Italian PET plastic industry, purity not reported)
Remarks: Procedure: Hela cells
Plates/test: Unknown
Activation system: S-9 was from Aroclor induced SD rats
Media: Phosphate-buffered saline
No. replicates: Unknown
Reference: Monarca, S., *et al.*, 1991.
Monarca, S., *et al.*, 1989.

D - Type: Chromosomal aberration

System of testing: Species/strain: Human PBL
Concentration: 50-500 µg/ml
Metabolic activation: With []; Without [X]; With and Without []; No data []

Results:

Cytotoxicity conc.: With metab. activation: NA
Without metab. activ.: Unknown

Precipitation conc.: Unknown

Genotoxic effects:

	+	?	-
With metab. activ.:	[]	[]	[]
Without metab. activ.:	[]	[]	[X]

Method: Lymphocytes (at stage G_0 of the cell cycle) were incubated with DMT for 4-hours at 37° C. DMSO was the solvent control and bleomycin was used as a positive control. Following DMT exposure, cells were cultured for 72-hours in RPMI media. Colcemid was added to the cultures 2-hours prior to harvesting. Coded slides were prepared and the cells were stained with a 4% Giemsa solution. Cells (100/subject) in metaphase were examined for frequency of chromatid and chromosomal gaps and breaks.

GLP: Yes []; No []; ? [X]
Test Substance: DMT (Italian PET plastic industry, purity not reported)
Remarks: Procedure: Human peripheral blood lymphocytes isolated from heparinized intravenous blood.
Plates/test: Unknown
Activation system: None
Media: RPMI 1640 supplemented with 20% fetal calf serum and phytohemagglutinin
No. replicates: Unknown
Reference: Monarca, S., *et al.*, 1991.
Monarca, S., *et al.*, 1989.

E - Type: Chromosomal aberration (micronuclei formation)
System of testing: Species/strain: Human PBL
Concentration: 50-500 µg/ml
Metabolic activation: With []; Without [X]; With and Without []; No data []

Results:

Cytotoxicity conc.: With metab. activation: NA
Without metab. activ.: Unknown

Precipitation conc.: Unknown

Genotoxic effects:

	+	?	-
With metab. activ.:	[]	[]	[]
Without metab. activ.:	[]	[]	[X]

Method: Lymphocytes were incubated with DMT and cultured in RPMI 1640 media. After 44-hours,

cytochalasin D was added and the cultures continued until 72-hours. After a mild hypotonic treatment, the cells were fixed and coded slides prepared for staining with Giemsa and scoring for micronuclei. One thousand cells were scored per subject for the presence of micronuclei.

GLP: Yes []; No []; ? [X]

Test Substance: DMT (Italian PET plastic industry, purity not reported)

Remarks: Procedure: Human peripheral blood lymphocytes isolated from heparinized intravenous blood.
Plates/test: Unknown
Activation system: None
Media: RPMI 1640 supplemented with 20% fetal calf serum and phytohemagglutinin
No. replicates: Unknown

Reference: Monarca, S., *et al.*, 1991.
Monarca, S., *et al.*, 1989.

F - Type: Unscheduled DNA synthesis (DNA amplification)

System of testing: Species/strain: Hamster/Syrian (embryo cells)

Concentration: 0, 2.5, 5.0, or 10.0 µg/ml

Metabolic activation: With []; Without [X]; With and Without []; No data []

Results:

Cytotoxicity conc.: With metab. activation: NA
Without metab. activ.: >10.0 µg/ml

Precipitation conc.: Unknown

Genotoxic effects:

	+	?	-
With metab. activ.:	[]	[]	[]
Without metab. activ.:	[]	[]	[X]

Method: Cells were grown in tissue flasks and plated onto microtiter plates. After 24-hours DMT (in DMSO) was added. After 96-hours of exposure, the cells were harvested and counted, and viability determined (trypan blue exclusion). AAV (adeno-associated virus) DNA content was detected by *in situ* hybridization. The survival index was determined by comparison to survival rates in the control wells. The amplification factor was calculated by comparing the extent of in situ hybridization of treated groups divided by the rate for the control group. A genotoxicity index was calculated by multiplying the survival index by the amplification factor and dividing the result by 100.

GLP: Yes []; No []; ? [X]

Test Substance: DMT (Italian PET plastic industry, purity not reported)

Remarks: Procedure: Syrian hamster embryo cells infected with adeno-associated virus (AAV type 2)

Plates/test: Unknown
Activation system: None
Media: Unknown
No. replicates: Unknown

Reference: Monarca, S., *et al.*, 1991.
Monarca, S., *et al.*, 1989.

G - Type: Gene mutation

System of testing: Species/strain: Mouse/L5178Y lymphoma cells (clone 3.7.2C.)

Concentration: 0-100 ug/ml

Metabolic activation: With []; Without []; With and Without [X]; No data []

Results:

Cytotoxic conc.: With metab. activ.: >100 ug/ml
Without metab. activ.: >100 ug/ml

Precipitation conc.: 75 ug/ml

Genotoxic effects:

	+	?	-
With metab. activ.:	[]	[]	[X]
Without metab. activ.:	[]	[]	[X]

Method: Increases in the frequency of 5-trifluorothymidine(TFT)-resistant cells due to mutational events occurring at the thymidine kinase locus following DMT exposure (50 µg/ml) was determined with and without S9 fraction. Dimethylformamide (1%) was used as the solvent carrier. The treatment period was 4 hours at 37^{o} C in a roller drum (10-15 rpm). Cells were retrieved by centrifugation and washed twice with growth media. The two-day expression and growth period was conducted with cell densities of $3x10^5$ cells/ml (20 ml of media on roller drum). After two-days, the cells were added to 90 ml of cloning media. Dishes containing the cells and cloning media were incubated for 11 to 12-days at 37° C with 5% CO_2/humidified air for colony development.

GLP: Yes []; No []; ? [X]

Test Substance: DMT (NTP Repository, 99% purity)

Remarks: Procedure: L5178Y mouse lymphoma cells (clone 3.7.2C.)
Plates/test: Unknown
Activation system: Aroclor 1254-induced male F344 rats
Growth media: RPMI 1640 medium supplemented with heat-treated horse serum (10% v/v), 220 µg/ml sodium pyruvate, 2 mM L-glutamine, 0.05% Pluronic F68 and gentamycin (50 µg/ml)
Treatment media: Fischer's growth medium with 5% heat-treated horse serum.

Cloning media: Growth media plus 0.35-0.40% agar and 3 µg/ml TFT
No. replicates: Unknown

Reference: Myhr, B.C. and Caspary, W.J., 1991.

H - Type: Chromosomal aberration and Sister chromatid exchange

System of testing: Species/strain: Chinese Hamster Ovary (CHO) cells

Concentration: 10 ug/ml

Metabolic activation: With []; Without []; With and Without [X]; No data []

Results:

Cytotoxic conc.: With metab. activ.: >10 ug/ml
Without metab. activ.: >10 ug/ml

Precipitation conc.: >10 ug/ml

Genotoxic effects:

	+	?	-
With metab. activ.:	[]	[]	[X]
Without metab. activ.:	[]	[]	[X]

Method: CHO cells were grown and treated under conditions similar to those described by Galloway *et al*., (1985). Aroclor-induced rat liver microsomal preparations were combined with cofactors and added as the metabolic activation system. Medium and solvent controls were used with each assay. Positive controls (Mitomycin C for use without the metabolic activation system and cyclophosphamide for use with the activation system) were also included. For sister chromatid exchange (SCE) experiments without metabolic activation, bromodeoxyuridine (BRDU) was added 2-hours after the addition of the control or test substance and the culture continued for 24-hours. Fresh medium with BRDU and colcemid replaced the previous media and the cultures continued for 2.5-hours. For SCE experiments with metabolic activation, serum free medium with cofactors, S9 fraction, and chemical were used for 2-hours and replaced with medium containing BRDU and the culture continued for 24-hours. Colcemid was added to the media and the cultures continued for 2.5-hours. The cells were then examined for cytotoxicity, harvested and fixed. Fluorescence-microscopy was then used to assess the frequency of metaphase cells and SCE. For experiments examining chromosomal aberrations without metabolic activation, media with either the control or test substance was used for 8-hours and then removed. Media containing colcemid replaced the previous media and the cultures continued for 2.5-hours. For experiments with metabolic activation,

serum free medium with cofactors, S9 fraction, and chemical were used for 2-hours, then the media removed and fresh media used for 8-hours. Colcemid was then added and incubations continued for 2-hours. Cells were harvested and slides prepared using a 5% Giemsa stain for five minutes. Two hundred cells per dose were scored for chromosomal aberrations.

GLP: Yes []; No []; ? [X]
Test Substance: DMT (NTP Repository, 99% purity).
Remarks: Procedure: CHO cells
Plates/test: Unknown
Activation system: Aroclor 1254-treated male SD rats
Media: McCoy's 5A (modified media) buffered with 20 mM HEPES and supplemented with 10% FBS, 2 mM L-glutamine, 50 IU penicillin, and 50 µg/ml streptomycin.
No. replicates: Unknown
Reference: Loveday, K.S., *et al.*, 1990.

I - Type: Transformation Assay
System of testing: Species/strain: Mouse BALB/c-3T3 cells
Concentration: 0.644 - 5.15 mM
Metabolic activation: With []; Without [X]; With and Without []; No data []

Results:
Cytotoxic conc.: With metab. activation: NA
Without metab. activ.: 5.15 mM
Precipitation conc.: Unknown
Genotoxic effects:

	+	?	-
With metab. activ.:	[]	[]	[]
Without metab. activ.:	[]	[X]	[]

Method: The transformation assay consisted of three components: a clonal survival assay, a co-culture clonal survival assay and a transformation assay. The first two were used to determine cytotoxic dose levels and determine effect of cell density on cytotoxicity. In the cell transformation portion, 18-20 vessels were seeded with 3.2×10^4 cells/vessel and exposed to 4 different levels of DMT for 48-hours. The number of type I-III transformed foci were identified using established criteria (3 phenotypic criteria: piling and overlapping cells, disorientation of cells at the periphery of the focus, and invasion of transformed cells into a contact-inhibited monolayer of WT cells. Two difficult technical problems arose. DMT was temperature sensitive and reacts with water. The solubility of the test material in the

media necessitated the use of a solubilizing agent, sonication of the media and heating to form a fine particulate suspension.

GLP: Yes []; No []; ? [X]
Test Substance: DMT
Remarks: Procedure: BALB/c-3T3 cells, (A31-1-13 clone)
Plates/test: 18-20/4 dose levels
Activation system: None
Media: Unknown
No. replicates: Unknown
Other: DMT was evaluated to have indeterminate activity in this assay due to the fact that the material was tested at levels that far exceeded its solubility in the culture medium.
Reference: Matthews, E.J., *et al*., 1993.

5.6. GENETIC TOXICITY IN VIVO

A.

Type: Sex-linked recessive lethality
Species/strain: *Drosophila melanogaster*/Canton-*S* (males)and *Basc* (females)
Sex: Female []; Male []; Male/Female [X]; No data []
Route of administration: Diet and injection
Exposure period: 72-Hours
Doses: 1,000 ppm (diet) and 400 ppm (injection)
Results:
Effect on mitotic Index or P/N ratio:
Genotoxic effects: + ? -
[] [] [X] Both exposure routes
Method: Males were fed DMT solutions for 72-hours and then mated to three virgin females for 3-days. After three-days, the exposed male was transferred to three virgin females for 3-days. This was repeated one additional time so that three broods were collected from each exposed male. The test was repeated using injections. To reduce the possibility of recovering multiple lethals from one male, no more than 100 F_1 females were mated over the three broods from any P_1 male. F_2 cultures were scored as presumptive lethals if the number of wild-type males were 0, 1, or <5% of the number of *Basc* males or *Basc*/+ females.

GLP: Yes []; No []; ? [X]
Test Substance: DMT (Aldrich 99% purity)
Remarks: None
Reference: Foureman, P., *et al.*, 1994.

B.	**Type:**	Chromosomal aberration (micronucleus assay)
	Species/strain:	Mouse/B6C3F1
	Sex:	Female []; Male [X]; Male/Female [X]; No data []
	Route of administration:	intraperitoneal injection
	Exposure period:	3-Days
	Doses:	438 to 1,750 mg/kg
	Results:	
	Effect on mitotic index or P/N ratio:	Control= 65% and 1,750mg/kg = 72%
	Genotoxic effects:	+ ? - [] [] [X]
	Method:	Mice (5-7) were exposed by ip injection to DMT (in a corn oil vehicle) over 3 consecutive days. The dose level used was the highest practical given the solubility problems with the test material. Animals were euthanized with CO_2 24-hours after their last exposure. Bone marrow smears (2 per mouse) were prepared and fixed with absolute methanol and stained with acridine orange. Each slide was evaluated for the number of micronuclei in polychromatic erythrocytes among 2,000 polychromatic erythrocytes and percentage of polychromatic erythrocytes among 200 erythrocytes.
	GLP:	Yes []; No []; ? [X]
	Test Substance:	DMT (NTP Repository, 99% purity)
	Remarks:	None
	Reference:	Shelby, M.D., *et al.*, 1993.
C.	**Type:**	Chromosomal aberration (micronucleus assay)
	Species/strain:	Mouse/(C57Bl/6j x CBA)F_1
	Sex:	Female []; Male [X]; Male/Female [X]; No data []
	Route of administration:	intraperitoneal injection
	Exposure period:	1-Day
	Doses:	0.20 to 1.00 mmole/kg
	Results:	
	Effect on mitotic index or P/N ratio:	Control= 41%, DMSO = 43% and 1 mmol/kg= 37%
	Genotoxic effects:	+ ? - [X] [] []
	Method:	A single 0.2 ml solution of DMT (dissolved in a DMSO vehicle) was injected intraperitoneally. The highest dose level used was limited due to the toxicity of the vehicle. Fifteen mice per exposure group were used, although lethality occurred in some animals, thereby reducing the sample sizes. Negative control groups (distilled water, or 0.2 ml

DMSO) and a positive control group (methylnitrosourea) were included. Mice were killed by cervical dislocation at 24, 48 and 72-hours post-treatment. Slides were prepared according to the method of Schmid (1976), dried at room temperature, and stained with May-Gruenwald and Giemsa stains. Polychromatic erythrocytes (1,000/mouse) were scored for the presence of micronuclei. After identifying 200 erythrocytes, the ratio of polychromatic erythrocytes to normochromatic erythrocytes was determined.

GLP: Yes []; No []; ? [X]

Test Substance: DMT (99% purity)

Remarks: The results of this study are particularly difficult to interpret. The data is not presented on a per mouse basis, but instead all of the data from the animals are lumped together as a group. Therefore, there is no mean and standard deviation for each group value. The distilled water negative control group (n=24) had a reported micronuclei frequency of 1.5%, although the time after treatment when this was determined was not reported. The use of DMSO as a solvent caused mortality in 21 of 270 mice after receiving either DMSO or DMSO and test material. The remaining live animals within each group were randomly selected to evaluate the micronucleus endpoint. The frequency of micronuclei in the DMSO negative control group decreases from 2.5% at 24-hours to 1.17% at 48-hours and further to 0.83% at 72-hours. The percentage of polychromatic erythrocytes in the DMSO solvent control group was significantly increased over the distilled water control group at 24-hours. Clearly the toxicity of DMSO was affecting the number of polychromatic erythrocytes and micronuclei in the DMSO solvent control group. All dose levels of DMT tested increased the frequency of micronuclei, although these findings were primarily restricted to the 24-hour observation point, coincidentally the time of greatest increase in micronuclei frequency due to the DMSO vehicle. The increased frequency of micronuclei at 48-hours were limited to the 3 highest dose levels tested and at 72-hours, the two highest dose levels tested. The highest dose was also considered to have caused bone marrow suppression. The pattern of the time course for micronuclei formation in the treated groups mimicked that observed for the DMSO vehicle

control, suggesting an interaction between the two chemicals (DMSO and DMT) may have occurred. Therefore, poor study design and reporting along with solvent toxicity makes interpretation of this study problematic. The dose levels tested were much lower than those used in other mouse micronuclei studies with a corn oil vehicle (3 injections over 3-days; above) and the increased frequency of micronuclei due to DMT treatment is in contrast to the other negative mutagenicity and clastogenicity findings for this material.

Reference: Goncharova, R.I., *et al.*, 1988.

D.

Type: Sex-linked dominant lethal assay
Species/strain: *Drosophila melanogaster*
Sex: Female []; Male []; Male/Female []; No data [X]
Route of administration: Ingestion from media
Exposure period: Unknown
Doses: Unknown (it was mentioned that the nutrient media was spiked with 0.3 mM of DMT)
Results:
Effect on mitotic Index or P/N ratio: NA
Genotoxic effects:

+	?	-
[X]	[]	[]

Method: Unknown
GLP: Yes []; No [X]; ? []
Test Substance: DMT
Remarks: The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.
Reference: Goncharova, R.I., *et al*., 1984.

5.7 CARCINOGENICITY

A.

Species/strain: Rat/F344 and Mouse/B6C3F1
Sex: Female []; Male []; Male/Female [X]; No data []
Route of administration: Diet
Exposure period: 2-Years
Frequency of treatment: 7-Days/week
Post Exposure observation period: 2-Weeks
Doses: 0, 2,500, or 5,000 ppm DMT
Control group: Yes [X]; No []; No data []; Concurrent no treatment [X]; Concurrent vehicle []; Historical [X]

Results:

Diet containing DMT at the above mention dose levels did not affect body weights, feed consumption, clinical signs, or survival. The bioassay report was issued twice in 1979. The first report concluded that DMT was carcinogenic in male mice due to an increased incidence of lung tumors in the low- and high-dose groups when compared to the matched controls. The matched control rate of lung tumors agreed with the historical control rate reported from the laboratory that conducted the study. DMT did not produce an increased incidence of any tumor types among male and female rats or among female mice. A draft of the first report was considered for peer review and was approved as written and released. The staff of the Carcinogenesis Testing Program of the National Cancer Institute (NCI) re-examined the data and reached the conclusion that the historical control rate of tumors to which the matched control group was compared was inappropriate for comparison since the historical control male mice came from studies of less than two-years duration. Since lung tumors are a late appearing tumor, the historical control rate for mice less than two years old would be expected to be low compared to that found in mice at two-years. The NCI staff then re-issued the report using "matched" control male mice lung tumor rates derived from other cancer bioassays conducted in the same room as the DMT bioassay at approximately the same time. The other male mice control groups housed concurrently with the male mice from the DMT bioassay had incidences of lung adenoma/carcinomas of 10% (5/49), 13% (6/46), and 18% (9/49) versus 4% (2/49) in control male mice in the DMT bioassay. Therefore, the lung tumor incidence in the male mouse control group in the DMT bioassay was considered "inordinately low". In addition, the majority (18/22) of the primary lung tumors found in the concurrent controls, were present in mice that survived to 104-weeks. The DMT control male mice had a survival rate of 64% (32/50) at that time point, while 82% and 78% of the low- and high-dose male mice (respectively) survived to 104-weeks. The lower survival rate (at two-years) of male control mice in the DMT bioassay may have been responsible for the low lung tumor incidence in that group. The re-issued report concluded that "The variability

evidenced by these control groups prevents an outright conclusion that the 13/49 (27%) incidence of lung tumors observed in the high dose male group in the (DMT) study is associated with the administration of the chemical." The Technical Report Summary concludes that DMT was not carcinogenic for F-344 rats or B6C3F1 mice under the conditions of the test. The revised report only had the abstract, statistical analysis, discussion and summary sections modified. The section dealing with the murine pathology (page 36) has the following statement "Based on histopathologic examination, a dose-related increase in primary tumors of the lung in male B6C3F1 mice may have been associated with long-term dietary administration of dimethyl terephthalate under the conditions of this bioassay." It is only in the statistical analysis section of the mouse bioassay report that the results are discussed.

On June 23, 1981, the Technical Reports Review Subcommittee of the NTP Board of Scientific Counselors conducted a peer review of the two reports. The re-issued report had been issued without an evaluation by a scientific review panel and the first report was considered incorrect based upon the arguments presented in the re-issued report.

In June 1981, NTP began 1) A re-examination and validation of the original diagnoses of lung tumors in the male mice, 2) A data analysis using the diagnoses of the pathologist performing the validation, and 3) presentation of the findings to the Technical Reports Review Subcommittee of the NTP Board of Scientific Counselors. The following conclusions were made by the Subcommittee: The original incidence of lung tumor was confirmed, however, the stage of tumor progression (adenoma vs. carcinoma) was questioned. Therefore, an analysis of the data was performed that considered the total lung tumor incidence rather than considering adenomas and carcinomas separately. Statistical analysis was done using the diagnosis of the validation pathologist by NTP/IARC recommended methods. Statistical comparisons included the incidences in both matched control and pooled control male mice. The conclusions out of this review were that

a statistically significant increase in total lung tumors was found for the high-dose group using either the matched-control or pooled-control incidences. However, this finding was considered biologically equivocal due to the following reasons: Lung tumors are relatively common in B6C3F1 mice, and the rate of incidence in the historical controls ranges from 2 to 34 percent. The 27% incidence rate found in the high-dose male mice in the DMT bioassay was within the high limit of the control range. Total lung tumor incidence is not dependent upon the sex of the mice and female mice had lung tumor incidences comparable to control values. Therefore, the observed lung tumor incidence in the male mice was considered less likely to be due to DMT exposure. The overall effect of the report revision followed by the re-interpretation by NTP in 1981 has been considerable confusion regarding the bioassay conclusions.

Method: A cancer bioassay was conducted on groups of 50 animals/species/sex. DMT was consumed in the diet for 104-weeks, followed by a 2-week observation period. At the end of the observation period the animals were necropsied and tissues examined histologically.

GLP: Yes []; No []; ? [X]

Test Substance: DMT (Technical grade obtained from Eastman Chemical Company. Analyzed by melting point, thin layer chromatography, elemental analysis, infrared, ultraviolet, visible and nuclear magnetic resonance spectra.)

Remarks: DMT has also been suggested to be a bladder carcinogen based on the 2-year bioassay results of one of the primary DMT metabolites, terephthalic acid (TPA). This suggestion is based upon the ability of high dietary concentrations of DMT to cause bladder stone formation following metabolism of DMT to TPA and excretion of the TPA in the urine. However, the NCI bioassay demonstrated no such effect (i.e. bladder stone formation or increase in urinary tract tumors or pathology). A possible reason as to why bladder stone formation was not found in the NCI bioassay was that although the dietary concentration of DMT used in the two-year studies was 0.25% and 0.5% it was still not sufficiently high enough to induce their formation.

Reference:	Federal Register (1981) "Public Health Service: Reevaluation by the National Toxicology Program of Technical Report NCI-CG-TRI-121 Entitled Bioassay of Dimethylterephthalate for Possible Carcinogenicity" FR 46(238):60654-60657. National Cancer Institute Technical Report Series "Bioassay of Dimethyl Terephthalate For Possible Carcinogenicity" (CAS No. 120-61-6, NCI-CG-TR-121, No. 121, 1979, revised summary)

5.8 TOXICITY TO REPRODUCTION

Type:	Fertility [X]; One generation study []; Two generation study []; Other []
Species/strain:	Rat/Long-Evans Hooded
Sex:	Female []; Male []; Male/Female [X]; No data []
Route of administration:	Oral, feed
Exposure period:	Males 115-days, Females 6-days prior to mating throughout gestation, parturition and lactation
Frequency of treatment:	7-Days/week (diet)
Post Exposure observation period:	Through weaning
Premating exposure period:	Males: 115-Days Females: 6-Days
Duration of test:	Through weaning of F1 animals
Doses:	0.25, 0.50, or 1.0%
Control group:	Yes [X]; No []; No data[]; Concurrent no treatment [X]; Concurrent vehicle []; Historical []
NOEL Parental:	1.0%
NOEL F1 Offspring:	0.25%
NOEL F2 Offspring:	NA
Results:	No signs of toxicity were observed in either the male or female parental animals (P). No effects were observed on fertility, reproductive capacity, libido, pregnancy, gestation, litter size, or offspring viability due to consumption of DMT. Pups born to parents fed 0.5 and 1.0% DMT had significantly lower average body weights at weaning when compared to the controls.
Method:	Males were fed DMT diets for 115-days. These males were then mated with virgin females that had been on test diets for 6 days. After mating, the pregnant females were fed the DMT diets throughout gestation, parturition and lactation.
GLP:	Yes []; No [X]; ? []
Test Substance:	DMT (Eastman Chemical Company, Cat. No. 6580)
Remarks:	The decreased weights observed at weaning are believed to be due to lactation exposure to the

DMT or its metabolite, TPA and access to treated diet. Studies with TPA have demonstrated an increased incidence of renal and bladder calculi formation in weanling animals when compared to adults consuming the same dietary level of terephthalic acid. This apparent increased sensitivity can be explained by the large amount of feed consumed in relation to body weight for young animals experiencing their initial growth spurt. Weanling animals are not more sensitive to terephthalic acid toxicity when the results are expressed on a mg/kg basis.

Reference: Krasavage, W.J., *et al.*, 1973.

B.

Type	:	other; one-generation
Species	:	Rat
Sex	:	male and female
Strain	:	CD and Wistar
Route of administration	:	oral; in feed
Exposure period	:	paternal: 90 days prior to and throughout mating maternal: 90 days prior to mating, throughout mating, gestation, and lactation offspring: 51 days; from birth through lactation and 30 days post weaning
Frequency of treatment	:	daily; in feed
Duration of test	:	approximately 160 days
Doses	:	0.03, 0.125, 0.5, 2.0, and 5.0%
Remark	:	The approximated mg/kg doses based on average feed consumption and body weight during the 90 day pre-mating period were: CD(M): 14, 59, 240, 930, 2499 CD(F): 17, 67, 282, 1107, 2783 Wistar(M): 14, 61, 249, 960, 2480 Wistar(F): 19, 78, 307, 1219, 3018
Control group	:	yes; concurrent no treatment
NOAEL Parental	:	0.5% (CD; Wistar: 2.0%)
NOAEL Reproductive	:	>5.0% (CD and Wistar)
NOAEL F1 Offspring	:	0.5% (CD and Wistar)
Method	:	other
Year	:	1982
GLP	:	Yes (see remark)
Test substance	:	terephthalic acid
Remark	:	No specific test material supplier or purity of test material was noted. A manager of quality assurance signed off on the study report. However, the report did not contain a specific statement *per se* in regard to the study being conducted under GLP assurances.

Result : Parental Effects: Following 90 days of exposure to TPA, statistically significant decreases in food consumption were observed in CD females treated with 2% and 5%, and in both sexes of Wistars treated with 5%.
Body weights were statistically decreased after 13 weeks in both sexes of CD rats on 2% and 5% TPA diets, and in males exposed to 0.03%. This effect occurred in Wistars (both sexes) only at the 5% level. There were 5 deaths (3 CD females, 1 Wistar/sex) reported during weeks 4-13 in animals given 5% TPA in the diet.
During the one-generation component of the study 3 CD (1 male at 2.0%, 1/sex at 5.0%) and 4 Wistar female (2 at 5.0% and 2 at 0.03%) rats died.
There was no effect of treatment on fertility index and litter size.

Offspring Effects: There were no effects of treatment on litter size, sex ratio, or total number of offspring. While no control offspring were found dead on Day 0, 17 Wistar pups (1 at 0.03%, 2 at 0.125%, 1 at 0.5%, 12 at 2.0% (2 from one dam and 10 from another)) and 23 CD pups (1 at 0.5%, 7 at 2.0% (3 dams) and 15 at 5.0% (3 dams; with 11 from one of them)) were found dead. No statistical differences were noted in viability on Days 0, 1, or 21 in either strain. In CD rats, survivability on Day 21 was reduced in both sexes of offspring whose parents had been exposed to 5% TPA in the diet.

In Wistar rats, body weights of both sexes of offspring from dams given 5.0% were reduced at Day 1. On Day 21, body weight was reduced in both strains of offspring from dams that ingested 5% TPA in the diet. Increased postnatal deaths on Day 1 and decreased survivability to Day 21 were noted in the 2% and 5% groups. At these dose levels, several large litters of pups were lost to dams suffering obvious signs of toxicity. Several of these dams did not allow the pups to nurse or attend to the litters. These pups were noted not to have milk in their stomachs and presented clinically as being very weak. These dams were consuming dietary levels of TPA known to cause reduced feed consumption, diarrhea and gastric trichobezoars (hairballs) and induce the formation of renal and bladder calculi. Unscheduled deaths during the postweaning period (Day 21-51) were confined to the 5% TPA group (18 Wistar and 16 CD) and were associated with a very high incidence of renal and bladder calculi. Renal and bladder calculi were noted in all animals exposed to 5% that were necropsied at Day 21. Day 51 necropsy findings also reported a very high incidence of renal and bladder calculi and the histological sequelae of the presence of the calculi.

Test condition : This study contrasted the toxicity of TPA in two different strains of rats. Experimental conditions were identical for both. Rats 15-17 weeks of age (n=30) were grouped housed 3/cage for the first 90 days of exposure. Body weight and feed intake were determined weekly during this time period. On Day 91, breeding pairs (n=10/sex) were housed together for 2 weeks prior to being separated. On Day 0 (delivery) the number and viability of offspring were evaluated and

grossly examined. Offspring were recounted, sexed, and weighed on Day 1. These measurements were repeated at weaning on Day 21. After weaning the litters were reduced to 2/sex/dose from each of 5 litters (20 pups/dose/strain) and maintained on test diets for 30 more days (Day 51) prior to sacrifice. There were only 9 pairs of CD strain rats at the 5% diet level. Remaining animals were necropsied within a few days post weaning. At termination offspring were grossly examined and necropsied. Parental and F1 generation animals were observed 2x/day for clinical signs. Body weight gain and standard reproductive indices were assessed and statistically compared using ANOVA and Dunnett's-t-test using SAS statistical programs. Parameters evaluated consisted of: fertility index, number of offspring born per dam; number and proportion of each sex born; number (Day 0, 1, and 21) and proportion (Day 1 and 21) of each sex alive; average weight at Day 1 and 21 of all offspring and of each sex.

Remark : Other studies have demonstrated an increased incidence of renal and bladder calculi formation in weanling animals when compared to adults consuming the same dietary level of TPA. This apparent increased sensitivity can be explained by the large amount of feed consumed in relation to body weight for young animals experiencing their initial growth spurt. Weanling animals are not more sensitive to TPA when the results are expressed on a mg/kg basis.

Conclusion : The NOAEL for reproductive toxicity was >5% in the diet (approximately 2480-3018 mg/kg/day). Whereas, the NOAEL for parental toxicity and the F1 generation was 0.5% TPA acid in the diet (approximately 240-307 mg/kg/day).

Reliability : (1) reliable without restriction

Reference : CIIT (1982) A Ninety-Day Study of Terephthalic Acid (CAS No. 100-21-0) Induced Urolithiasis and Reproduction Performance in Wistar and CD Rats. CITI Docket 11622

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

A.	**Species/strain:**	Rat
	Sex:	Female [X]; Male []; Male/Female []; No data []
	Route of administration:	Inhalation
	Duration of test:	Throughout gestation
	Exposure period:	Unknown
	Frequency of treatment:	Unknown
	Doses:	1 mg/m^3
	Control group:	Yes [X]; No []; No data[]; Concurrent no treatment [X]; Concurrent vehicle []; Historical []
	NOEL Maternal Toxicity:	1 mg/m^3

	NOEL Teratogenicity:	1 mg/m^3
	Results:	No abnormal developmental effects and no pre- or post-implantation losses were noted.
	Method:	Inhalation - Thirty pregnant rats were exposed to 1 mg/m^3 of DMT throughout gestation.
	GLP:	Yes []; No [X]; ? []
	Test Substance:	DMT
	Remarks:	The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.
	Reference:	Krotov, Y.A. and Chebotar, N.A., 1972.
B.	**Species/strain:**	Rat/Wistar
	Sex:	Female [X]; Male []; Male/Female []; No data []
	Route of administration:	Oral gavage
	Exposure period:	Gestation days 7-16
	Frequency of treatment:	single daily exposure
	Doses:	1000 mg/kg
	Control group:	Yes [X]; No []; No data[]; Concurrent no treatment [X]; Concurrent vehicle []; Historical []
	NOEL Maternal Toxicity:	>1000 mg/kg
	NOEL Teratogenicity:	>1000 mg/kg
	Results:	No abnormal developmental effects and no pre- or post-implantation losses were noted. No maternal effects were noted.
	Method:	Unknown, anaimals were sacrificed on Day 21.
	GLP:	Yes []; No []; ? [X]
	Test Substance:	DMT
	Remarks:	The design, conduct, and data interpretation of this study cannot be evaluated due to the lack of the primary reference, and is limited by the lack of detail in the report.
	Reference:	Hoechst 1986
C.	**Species:**	Rat
	Sex:	Female
	Strain:	Sprague-Dawley
	Route of admin.:	Inhalation
	Exposure period:	days 6-15 of gestation
	Frequency of treatment:	6 hours/day for 10 consecutive days
	Duration of test:	20 days
	Doses:	1.0, 5.0, and 10.0 mg/m^3
	Control group:	yes; filtered room air
	NOAEL Maternal:	>10.0 mg/m^3
	NOAEL Fetal:	>10.0 mg/m^3
	Method:	Other
	Year:	1989

GLP:	Yes
Test substance:	as prescribed by 1.1-1.4
Remark:	Test material was supplied by the Amoco Corporation. Purity was not noted but typically exceeds 99%. Respirable time-weighted average concentrations were 0.90, 4.73, and 10.4 mg/m^3.
Result:	Maternal Effects: No mortalities occurred in any group. The incidences of clinical signs observed in rats exposed to TPA were similar to controls. No statistically significant differences were noted in mean dam body weight or weight gain, uterine weight, or implant number. Fetal Effects: No statistically significant differences were noted in mean litter weights, pup viability, or number of fetal malformations. External soft tissue examinations did not indicate any differences from control. However, internal examinations showed a slight increase in the incidence of rib anomalies in the middle dose (5.0 mg/m^3) group. This was only significant when all the various types of rib anomalies were added together.
Remark:	Rib anomalies were not deemed to be an indicator of teratogenesis because they were common variations, were not elevated in a dose-related manner, and occurred at a rate that was within the range of the laboratories own historical controls. Furthermore, no other signs of embryotoxicity were associated with this change.
Test condition:	Female rats weighing 117-150 g were quarantined and housed 2/cage with 1 male. Confirmation of mating was via evidence of sperm in a vaginal smear (Day 0), after which females were housed singly. The study consisted of 26-27 timed-pregnant dams per dose level. Exposures were by whole body inhalation conducted in 2 m^3 chambers with an airflow rate of 305-420 l/min. Test article was ground to respirable-sized particles using a Retsch Ultra-Centrifugal Mill. Chambers were sampled 2x/exposure period and TPA levels were determined by spectrophotometric analysis. Particle size was determined using a cascade impactor. Temperature, humidity and airflow were measured hourly. Animals were observed twice daily and given detailed physical exams daily on days 0 and 6-20. Dams were weighed on Days 0, 5 (randomization into groups), 6 (exposure initiation), 11, 16, and 20 (study termination). Standard "guideline" postmortem procedures were carried out on the females and their fetuses. Data were analyzed in an appropriate statistical manner using log transformations, multivariate ANOVA, single factor ANOVA and Dunnett's-"t"-test depending on the

	nature and type of end-point assessed. The dam was considered to be a random factor and the pup a nested factor within the dam.
Reliability:	reliable without restriction
Reference:	Amoco Corporation (1989) and Ryan BM, et al. (1990).

5.10 OTHER RELEVENT INFORMATION

A. SPECIFIC TOXICITIES

Type:	(neurotoxicity, immunotoxicity, etc.)
Results:	No studies located
Remarks:	
Reference:	

B. TOXICODYNAMICS, TOXICOKINETICS

A -	**Species/strain**:	Rat
	Method:	Animals were fed diets containing 5% DMT for five-days
	Results:	DMT was reported to almost be completely absorbed and primarily eliminated by the kidney. Only a trace amount was found to be excreted unchanged in the urine; the rest is metabolized to terephthalic acid. About 15% of the unabsorbed ester appears in the feces; the balance is probably also destroyed by the intestinal flora.
	GLP:	Yes []; No [X]; ? []
	Test Substance:	DMT
	Remarks:	Interpretation of the study is limited by the lack of detail in the report.
	Reference:	Du Pont Co., Haskell Laboratory, unpublished data, MR-468-1, HL-55-58.
B -	**Species/strain:**	Rat/Charles River and Rabbit/New Zealand albino (used only for the studies using ocular administration)
	Method:	A 1% Triton-X-100 solution in water was used as a vehicle for the ocular, intratracheal, and dermal studies. The relative insolubility of DMT in the aqueous vehicle presented problems with dosing samples and storage of dosing solution. Probe sonification was used to suspend the DMT within the solution. Peanut oil was used as a vehicle in the oral studies. Ocular administration - Eight albino rabbits were used to test the absorption and excretion of DMT

following ocular administration. A single 50 mg dose of C^{14}-labeled DMT (20 μCi/dose) was instilled into the conjunctival sac of one eye of each rabbit. Group I (5 animals) was exposed for five minutes after which the eyes were washed with copious amounts of distilled water and examined. Group II (3 animals) was exposed for 24-hours after which the eyes were washed with copious amounts of distilled water and examined. All rabbits were sacrificed 10-days after dosing.
Dermal administration - Doses were applied in 0.2 ml of vehicle to unabraded depilated dorsal skin of rats. The study used a single dose/day of 80 mg of C^{14}-DMT either for one-day (single dose) or for five doses over a 10-day period (one every other day). The same area of skin was used for dosing in the repeat dose dermal study and covered with a gauze patch in between dose administrations. In order to determine the total dose applied to the skin, the gauze patches were counted for residual radioactivity at the completion of the study.

Intratracheal administration - Parameters following intratracheal administration were measured using groups of five rats with either a single dose or five doses (one every other day) over a 10-day period. Dose levels were 0, trace (4 μCi), 5 mg, or 10 mg.

Oral administration - Parameters following oral exposure were measured using groups of five rats with either a single oral dose or five oral doses (one every other day) over a ten-day period. Oral dose levels were 0, trace (4 μCi), 20 mg, or 40 mg. Each dose contained 4 μCi tracer with or without added carrier compound.

Results:

Ocular administration - Approximately 29% of the C^{14}-label was recovered in the urine of rabbits receiving the five minute exposure and 37% of the dose was recovered following the 24-hour exposure. Fecal excretion was minimal. Examination of internal organs for C^{14}-label revealed only 0.1% remaining ten-days after the exposure.

Dermal administration - Approximately 11% of the C^{14}-label was recovered in the urine and feces in the 10-days following the single dermal exposure. Approximately 13% of the C^{14}-label were recovered in the urine and feces over the 10-day dosing period with the repeated dermal exposure. No evidence of

skin irritation occurred during the single or repeated dermal administrations.

Intratracheal administration - Total excretion (urine and feces) of a tracer dose of C^{14}-labeled DMT at the 24-hour time point after a single intratracheal administration was 53% of the total dose. Similar results (62%) were obtained at 48-hours. C^{14}-label in the urine was 52-58% of the total dose, and the feces contained 1.8-3.2% of the total dose. C^{14}-label remaining after repeated administration revealed less than 1% of the total dose remaining in the lungs and tracheal lymph nodes at 24-hours after the last administration. Negligible radioactivity (<0.1%) was found in all the other organs assayed. The largest percentage of the total radioactivity was recovered from the urine and smaller amounts in the feces after repeated dosing.

Oral administration - Greater than 83% of a single dose of C^{14}-labeled DMT was excreted within 48-hours post-dosing. The urine contained approximately 86% of the administered dose at 48-hours. Less than 10% of the radiolabel was in the feces at that time point. After dosing five times over a 10-day period, greater than 91% of the total administered dose was recovered from feces and urine within 24-hours of the final dose.

GLP: Yes []; No [X]; ? []

Test Substance: DMT - uniformly ring-labeled with Carbon-14 (obtained from Mallinckrodt Chemical Works, St. Louis, Missouri) and unlabeled DMT (Matheson Scientific Company, Cincinnati, Ohio)

Remarks: Overall, the data indicate that there is no significant bioaccumulation of DMT within the organism, even with repeated administration. Preliminary solvent extraction experiments with the feces and urine revealed a major portion of the radioactivity within the water-soluble fraction suggesting metabolism to more water soluble compounds.

Reference: Moffitt, A.E. Jr., *et al*. 1975.

C - Species/strain: Rat/F344 and Mouse/B6C3F1

Method: Male rats and mice received a single oral dose of C^{14}-DMT (ring-labeled). Urine and feces were collected over a 48-hour period for metabolite identification using reverse-phase HPLC.

Results: Urinary and fecal excretion accounted for 90% and 10% of the dose, respectively, in both species. Less

than 1% remained in the carcass after 48 hours. In the rat, terephthalic acid (TPA) was the only compound detected in the urine. While in mice, urinary metabolites consisted of monomethyl terephthalate (70%), TPA (30%) and traces of DMT. Similar metabolites were identified in the feces of both species. The possibility that DMT might lower the concentration of nonprotein sulfydryl groups also yielded negative results. Thus, demonstrating DMT is not activated to form electrophilic metabolites.

GLP: Yes []; No [X]; ? []
Test Substance: DMT (C^{14}-DMT; ring-labeled).
Remarks: None
Reference: Heck, H. d.'A., 1980.

D - Species/strain: Rat/F344
Method: Female rats (4/group) were fed diets containing 0, 1.0 or 2.0% DMT for three weeks. Fresh samples of urine were collected from each animal over the three-week exposure period. Urinary pH, electrolyte composition, and terephthalic acid concentrations were determined.
Results: Female F-344 rats fed diets containing 0, 1.0 or 2.0% DMT developed hypercalciuria and urinary acidosis. Metabolism of DMT to terephthalic acid (TPA) was demonstrated. The counter ion for urinary TPA appeared to be ammonium.
GLP: Yes []; No [X]; ? []
Test Substance: DMT
Remarks: None
Reference: Heck, H. d'A. and Kluwe, C.L., 1980.

C. OTHER

Risk Assessment Review:

Calcium terephthalate (Ca-TPA) is the major component of bladder stones induced by DMT in rats. Based on urinary solubility of Ca-TPA, normal human urine would become saturated with Ca-TPA at a TPA concentration of approximately 8 to 16 mM. Assuming that the average volume of urine excreted by man is 1.5 L/day and that DMT is metabolized entirely to TPA, the amount of DMT that would have to be absorbed to produce the minimum saturating concentration of TPA (8 mM) is 2,400 mg/day.

Remarks: A value of 2,400 mg/day is found in the reference. However, using a molecular weight of 194.2 x 8 mM x 1.5 L of urine per day I calculate the minimum daily dose to be 2,330 mg. This value is very conservative as it assumes 100% conversion of DMT to TPA and a similar quantitative excretion in the urine in one day.

Reference: Heck, H. d'A., and Tyl, R.W., 1985.

5.11 EXPERIENCE WITH HUMAN EXPOSURE

A.

Results: An oily paste containing 80% DMT showed no irritant effects 24-hours after 10 applications to human skin.

Remarks: Interpretation of this report is limited due to a sparseness of detail in the report and a lack of the primary reference.

Reference: Massmann, W., 1966.

B.

Results: A Russian study reports no adverse effects in workers exposed to high concentrations of DMT.

Remarks: Interpretation of this report is limited due to a sparseness of detail in the report and a lack of the primary reference.

Reference: Korbakova, A.I., 1964.

C.

Results: A Russian study reported moderate leukocytosis in workers involved in synthesis of DMT

Remarks: These workers were also exposed to other chemicals. Interpretation of this report is limited due to a sparseness of detail in the report and a lack of the primary reference.

Reference: Kamal'dinova, Z.M., *et al*., 1962.

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IUCLID DATASET FOR

DIMETHYL TEREPHTHALATE (CAS RN 120-61-6)

I U C L I D

D a t a s e t

Existing Chemical	Substance ID: 120-61-6
CAS No.	120-61-6
EINECS Name	dimethyl terephthalate
EINECS No.	204-411-8
Molecular Formula	C10H10O4

Dataset created by: EUROPEAN COMMISSION - European Chemicals Bureau

This dossier is a compilation based on data reported by the European Chemicals Industry following 'Council Regulation (EEC) No. 793/93 on the Evaluation and Control of the Risks of Existing Substances'. All (non-confidential) information from the single datasets, submitted in the IUCLID/HEDSET format by individual companies, was integrated to create this document.

The data have not undergone any evaluation by the European Commission.

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1.0.1 OECD and Company Information

Name: Hoechst AG
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Town: 65903 Frankfurt/Main
Country: Germany

Name: Hoechst Trevira GmbH & Co KG
Town: 65926 Frankfurt am Main
Country: Germany

Name: Huels AG
Street: Postfach
Town: D-45764 Marl
Country: Germany

Name: INTERCONTINENTAL QUIMICA, S.A.
Street: PASEO CASTELLANA,141 10-AD
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Name: MONTEFIBRE S.p.A.
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Town: 20124 Milan
Country: Italy
Phone: 02/6977/1
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Name: Rhone-Poulenc Chimie
Street: 25, Quai Paul Doumer
Town: 92408 Courbevoie Cedex
Country: France

1.0.2 Location of Production Site

-

1.0.3 Identity of Recipients

-

1.1 General Substance Information

Substance type: organic
Physical status: solid

1.1.1 Spectra

-

1.2 Synonyms

1,4-Benzenedicarboxylic acid, dimethyl ester
Source: Huels AG Marl

1,4-Benzoldicarbonsaeure-dimethylester
Source: Huels AG Marl

Benzol-1,4-dicarbonsaeure-dimethylester
Source: Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

DIMETHYL TEREPHTALATE
Source: Rhone-Poulenc Chimie Courbevoie Cedex

DIMETHYL TEREPHTALATE FONDU
Source: Rhone-Poulenc Chimie Courbevoie Cedex

Dimethyl-1,4-benzenedicarboxylate
Source: Huels AG Marl

Dimethyl-p-phthalat
Source: Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

Dimethylterephthalat
Source: Hoechst AG Frankfurt/Main
Huels AG Marl
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

DMT
Source: Hoechst AG Frankfurt/Main
Huels AG Marl
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

DMT, DIMETHYLTEREPHTHALATE
Source: MONTEFIBRE S.p.A. Milan

Terephthalic acid dimethylester
Source: Huels AG Marl

Terephthalsaeure-dimethylester
Source: Huels AG Marl

Terephthalsaeuredimethylester
Source: Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

1.3 Impurities

-

1.4 Additives

-

1.5 Quantity

Quantity more than 1 000 000 tonnes

1.6.1 Labelling

-

1.6.2 Classification

-

1.7 Use Pattern

Type: type
Category: Non dispersive use

Type: type
Category: Use in closed system

Type: industrial
Category: Chemical industry: used in synthesis

Type: use
Category: Intermediates

1.7.1 Technology Production/Use

-

1.8 Occupational Exposure Limit Values

Type of limit: MAK (DE)
Limit value:
Country: Germany
Remark: MAK-Wert: not established
Source: Huels AG Marl

(1)

Type of limit:
Limit value: 10 mg/m3
Short term expos.
Limit value: 5 mg/m3
Schedule: 8 hour(s)
Frequency: 40 times
Remark: Tipo de límite.- Nivel de exposición ambiente en el puesto de trabajo.
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Type of limit:
Limit value:
Remark: DMT is produced in closed system. In our plant maximum concentration in air of workplace is 0.07mg/m3.
Source: MONTEFIBRE S.p.A. Milan

1.9 Source of Exposure

Memo: Emissionserklaerung Huels 1992
Remark: Release into the atmosphere on production site in 1992: 110 kg/a
Source: Huels AG Marl

(2)

Remark: Procede de production :

Oxydation du Para-xylene en acide terephtalique par injection d'air sous 6 bar. Puis esterification par le methanol en dimethyl terephtalate (DMT).
Ensuite le DMT est purifie successivement par cristallisation et distillation.

Rejets aqueux et dechets :

- Production moyenne de 200 T/jour par tonne de DMT produite.

- Les rejets aqueux (37.5 kg/jour de DCO par tonne produite) sont envoyes dans une station biologique qui fonction avec un rendement de 83 %.

- Les dechets (158 kg/jour de DCO par tonne produite) sont tous incineres :
. Les liquides (98 %) sur place dans un four.
. Les solides (2 %) a l'exterieur.

Rejets atmospheriques :

AIR appauvri sortant des oxydeurs charge legerement de carbone organique volatil (COV).
Source: Rhone-Poulenc Chimie Courbevoie Cedex

Remark: Our production is performed in closed system and the chemical is 100% intermediate. It is used in the same factory, or others, only for preparation of the ¿polyester polymer (no public use).
Source: MONTEFIBRE S.p.A. Milan

1.10.1 Recommendations/Precautionary Measures

-

1.10.2 Emergency Measures

-

1.11 Packaging

-

1.12 Possib. of Rendering Subst. Harmless

-

1.13 Statements Concerning Waste

-

1.14.1 Water Pollution

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 1 (weakly water polluting)
Source: Hoechst AG Frankfurt/Main

(3) (4)

Classified by: KBwS (DE)
Labelled by:
Class of danger: 1 (weakly water polluting)
Remark: Selbsteinstufung
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(3) (5) (4)

Classified by: other: Huels AG
Labelled by: other: Huels AG
Class of danger: 1 (weakly water polluting)
Country: Germany
Source: Huels AG Marl

(1)

1.14.2 Major Accident Hazards

Legislation: Stoerfallverordnung (DE)
Substance listed: no
Country: Germany
Remark: Stoerfallverordnung 1991
Source: Huels AG Marl

(1)

1.14.3 Air Pollution

Classified by: TA-Luft (DE)
Labelled by:
Number: 3.1.7 (organic substances)
Class of danger: III
Remark: Als staubförmiges Material nach '3.1.3 Gesamtstaub' zu begrenzen
Selbsteinstufung
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(6)

Classified by: other: Huels AG
Labelled by: other: Huels AG
Number: 3.1.7 (organic substances)
Class of danger: III
Country: Germany
Source: Huels AG Marl

Classified by: other: Selbsteinstufung
Labelled by: TA-Luft (DE)
Number: 3.1.7 (organic substances)
Class of danger: III
Remark: Als staubförmiges Material nach '3.1.3 Gesamtstaub' zu begrenzen
Source: Hoechst AG Frankfurt/Main

(6)

1.15 Additional Remarks

Remark: - Transport par camion-citerne calorifuge : +- 40 KT/an.

- Risques majeurs d'accident :

  Le procede n'est pas concerne par la Directive Seveso.
Pas de substance listee.

Les risques majeurs mis en evidence entrent dans le cadre du plan d'operation interne.
Source: Rhone-Poulenc Chimie Courbevoie Cedex

Remark: The product coming from incidental losses is generally recycled in the same plant. Possible wastes are disposed sending to suitable incinerator.
Source: MONTEFIBRE S.p.A. Milan

1.16 Last Literature Search

-

1.17 Reviews

-

1.18 Listings e.g. Chemical Inventories

-

2.1 Melting Point

Value: = 140 degree C
Decomposition: no
Sublimation: no
Method: other
GLP: no data
Source: MONTEFIBRE S.p.A. Milan
(7)

Value: ca. 140 degree C
Decomposition: no
Sublimation: no
GLP: no
Source: Huels AG Marl
(8) (9) (10) (11) (12)

Value: 140.6 degree C
Source: Huels AG Marl
(13) (14)

Value: = 140.6 degree C
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15) (5)

Value: 141 - 141.8 degree C
Source: Huels AG Marl
(16) (17)

Value: = 141 degree C
Sublimation: yes
Method: other
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Value: 141 degree C
Source: Huels AG Marl
(18)

2.2 Boiling Point

Value: = 282 degree C at 1013 hPa
Decomposition: no
Method: other: DIN 51751
GLP: no data
Source: Huels AG Marl
(13) (14) (11)

Value: = 284 degree C
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Value: = 284 degree C at 1013 hPa
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15) (5)

Value: 285 degree C at 1013 hPa
Source: Huels AG Marl
(17)

Value: > 400 degree C at 1013 hPa
Decomposition: yes
Remark: Thermische Zersetzung
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15) (5)

Value:
Decomposition: yes
Method: other
GLP: no data
Remark: SUBLIMES BEFORE BOILING AT 300°C AND 101.3KPa.
Source: MONTEFIBRE S.p.A. Milan
(7)

2.3 Density

Type: density
Value: = 1 - 283 kg/m3 at 20 degree C
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Type: density
Value: = 1.04 g/cm3 at 20 degree C
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15) (5)

Type: density
Value: = 1.35 g/cm3 at 20 degree C
Method: other: DIN 51757
GLP: no
Source: Huels AG Marl
(19)

Type: density
Value: = 1.084 g/cm3 at 150 degree C
Method: other: DIN 51757
GLP: no
Source: Huels AG Marl
(11)

Type: relative density
Value: = 1.04
Method: other
GLP: no data
Source: MONTEFIBRE S.p.A. Milan
(20)

Type: bulk density
Value: ca. 500 kg/m3
GLP: no
Source: Huels AG Marl
(19)

Type: bulk density
Value: = 500 kg/m3
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15) (5)

2.3.1 Granulometry

-

2.4 Vapour Pressure

Value: < .02 hPa at 20 degree C
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15)

Value: < .13 hPa at 30 degree C
Source: Huels AG Marl
(13) (18)

Value: 1.53 hPa at 93 degree C
Source: Huels AG Marl
(8) (13)

Value: = 21 hPa at 100 degree C
Method: other (measured)
GLP: no data
Source: MONTEFIBRE S.p.A. Milan
(21)

Value: 11.6 hPa at 140 degree C
Source: Huels AG Marl
(14)

Value: < 1 hPa at 140.6 degree C
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(5)

Value: ca. 18 hPa at 150 degree C
GLP: no
Source: Huels AG Marl
(11)

Value: 26.2 hPa at 160 degree C
Source: Huels AG Marl
(14)

Value: 108.8 hPa at 200 degree C
Source: Huels AG Marl
(14)

Value: = 133 - 0 hPa at 210 degree C
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Value: 363.8 hPa at 240 degree C
Source: Huels AG Marl
(14)

2.5 Partition Coefficient

log Pow: = 1.66
Method: other (calculated): KOWWIN v1.35a, Syracuse Research Corporation, EnvironmentalSciences Center, Merill Lane, Syracuse, NY 13210
Year: 1994
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(22)

log Pow: = 2.35 at 20 degree C
Method: other (measured)
Year: 1993
GLP: yes
Remark: ANALYTICAL METHOD: EEC A8 - MOS/PHC/001
Source: MONTEFIBRE S.p.A. Milan

log Pow: = 2.36
Method: other (calculated): Leo, Hansch: Berechnung mit dem MedChem-Programm, Version 1989 (POMONA89)
Year: 1989
Source: Huels AG Marl

log Pow: = 2.4 at 23 degree C
Method: OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year: 1981
GLP: no
Source: Huels AG Marl
(23)

2.6.1 Water Solubility

Value: < .5 g/l at 20 degree C
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15) (5)

Value: = 28.7 mg/l at 20 degree C
pH: = 5.9 and 20 degree C
Method: other
Year: 1993
GLP: yes
Remark: ANALYTICAL METHOD: EEC A6 - MOS/PHC/019
Source: MONTEFIBRE S.p.A. Milan

Value: = 36 mg/l at 20 degree C
Qualitative: of very low solubility
GLP: no
Source: Huels AG Marl

(11)

Remark: Solubilidad en agua: Negligible.
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

2.6.2 Surface Tension

-

2.7 Flash Point

Value: 140 degree C
Type: other
Method: other: offener Tiegel
Year:
Source: Huels AG Marl

(8)

Value: = 141 degree C
Type: closed cup
Method: other: DIN 51758
Year:
GLP: no
Source: Huels AG Marl

(11)

Value: = 146 degree C
Type: open cup
Method: other
Year:
GLP: no data
Remark: METHOD: CLEVELAND
Source: MONTEFIBRE S.p.A. Milan

(24)

Value: 146 degree C
Type:
Method:
Year:
Source: Huels AG Marl

(17)

Value: 154 degree C
Type:
Method:
Year:
Method: keine Angabe
Source: Huels AG Marl
(9)

Value: ca. 154 degree C
Type: closed cup
Method: other: DIN 51758
Year:
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15) (5)

Value: = 519 degree C
Type:
Method: other
Year:
Remark: Método: ASTM D-2155
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

2.8 Auto Flammability

Value: = 500 degree C
Method: other: DIN 51794
Remark: Zündtemperatur
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15) (5)

Value: = 570 degree C
Method: other
GLP: no data
Source: MONTEFIBRE S.p.A. Milan
Test condition: 570°C AS A DUST CLOUD (IGNITION)
(25) (26)

Value: = 680 degree C
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15)

2.9 Flammability

Result: flammable
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Result: other
Remark: Entwicklung zündfähiger Gemische möglich in Luft bei Erwärmung über dem Flammpunkt und/oder beim Versprühen oder Vernebeln.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(5)

Result:
Source: MONTEFIBRE S.p.A. Milan

2.10 Explosive Properties

Result: not explosive
Source: MONTEFIBRE S.p.A. Milan
Test condition: EXPLOSIVITY IN AIR : LOWER LIMIT = 0.03 g/l.
(27)

Result:
Remark: Concentraciones de polvo de más de 0.030 g/litro en una atmósfera con, al menos, 12% vol. de O2, pueden formar una mezcla inflamable. Cuando se maneja polvo es posible la acumulación de electricidad estática de alto voltaje. Por lo tanto, se aconseja encarecidamente tomar las precauciones adecuadas, incluyendo una completa interconexión y puesta a tierra del equipo, así como la inertización con un gas inerte (menos del 10% vol O2).
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

2.11 Oxidizing Properties

-

2.12 Additional Remarks

Remark: El material fundido produce severas quemaduras térmicas. Por lo tanto, si se utiliza agua para controlar un fuego de DMT fundido, mantenerse alejado a distancia segura.
Cuando se le somete a alta temperatura o arde se forman los siguientes productos:
- Monóxido de Carbono (CO).
- Dióxido de carbono (CO2).
- Agua.
No se forman productos peligrosos cuando entra en contacto con el agua.
Reactividad.- No hay materiales cuyo contacto con el producto deba ser evitado especialmente.
Estabilidad.- No se producen polimerizaciones peligrosas.
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Remark: ignition temperature: 500 Grad C
Source: Huels AG Marl
(9)

Remark: ignition temperature: 520 degree C (DIN 51794)
Thermal composition above 400 degree C.
Explosions may occur when solid is suspended in air.
lower explosion limit: 1,8 Vol.%
Source: Huels AG Marl
(13) (19)

Remark: Brennbarkeit: Brennzahl BZ2 (Kurzes Aufflammen ohne Ausbreitung)
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15)

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500000 molecule/cm3
Rate constant: = .0000000000005742 cm3/(molecule * sec)
Degradation: = 50 % after 27.9 day
Method: other (calculated): AOP Computer Program, Vers. 1.53, Syracuse Research Center (based on Reference)
Year: 1994 **GLP:**
Test substance:
Remark: The OH concentration represents 24 hour average, thus the half-life refers to 24 hour-days.
Source: Huels AG Marl

(28)

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 1500000 molecule/cm3
Rate constant: = .0000000000005742 cm3/(molecule * sec)
Degradation: ca. 50 % after 18.6 day
Method: other (calculated): AOPWIN v1.55a, Syracuse Research Corporation, Chemical HazardAssessment Division, Merill Lane, Syracuse, NY 13210
Year: 1994 **GLP:**
Test substance:
Remark: Die Sensibilisatorkonzentration bezieht sich auf eine durchschnittliche Konzentration der OH-Radikale über einen Zeitraum von 12 Stunden Tageslicht.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(22)

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500000 molecule/cm3
Rate constant: = .0000000000005742 cm3/(molecule * sec)
Degradation: ca. 50 % after 27.9 day
Method: other (calculated): AOPWIN v1.55a, Syracuse Research Corporation, Chemical HazardAssessment Division, Merill Lane, Syracuse, NY 13210
Year: 1994 **GLP:**
Test substance:
Remark: Die Sensibilisatorkonzentration bezieht sich auf eine durchschnittliche Konzentration der OH-Radikale über einen Zeitraum von 24 Stunden.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(22)

3.1.2 Stability in Water

Type:
Method:
Year: **GLP:**
Test substance:
Remark: Es biodegradable.
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

3.1.3 Stability in Soil

-

3.2 Monitoring Data (Environment)

Type of measurement:
Medium:
Remark: Protección ambiental.-
Se sabe que el producto es biodegradable. Su bioacumulación en varias especies es, todavía, objeto de investigación, pero, presumiblemente es muy baja.
Dado que cualquier derrame de producto, cuando se le transporta en estado fundido, solidifica rápidamente y que el DMT tiene muy baja solubilidad en agua, el riesgo de daños al Medio Ambiente a causa de un derrame accidental, es mínimo.
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

3.3.1 Transport between Environmental Compartments

-

3.3.2 Distribution

Media: air - biota - sediment(s) - soil - water
Method: other (calculation)
Year: 1993
Method: ENICHEM COMPUTER PROGRAM by GARLANDA T. and MASOERO M.
Remark: Theoretical distribution between environmental compartments calculated on a global basis . The model represents a steady-state partitioning, not including reaction or interphase transport. Applications and limitations are the same as for a fugacity model of I level. In the present case the ratio between the soil-water areas is 70/30.
Result: Percent in air : 84.8
Percent in water : 14.5
Percent in sediment : 0.34
Percent in soil : 0.30
Source: MONTEFIBRE S.p.A. Milan
Test condition: Molecular Mass : 194.18
Melting point : 140°C
Water solubility : 28.7 mg/l
Vapor pressure (calculated) : 2.5 Pa a 25°C
Temperature : 298 °Kelvin

log Kow : 2.35

Media: air - biota - sediment(s) - soil - water
Method: Calculation according Mackay, Level I
Year:
Result:

Air:	82.009 %
Soil:	0.361 %
Water:	17.293 %
Sediment:	0.337 %
Biota:	0.000 %

Source: Huels AG, Marl
Huels AG Marl
Test condition: Data used:

Molar mass:	194.19 g/mol
log Pow	2.40
Vapour pressure:	2.5 Pa
Water solubility:	0.036 g/l

Equations used for additional data:
log Koc = 0.989 log Pow - 0.346

Volumes used:

Air	6 000 000 000
Soil:	45 000
Water:	7 000 000
Sediment:	35 + 21 000
Biota:	7

3.4 Mode of Degradation in Actual Use

-

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge, domestic
Concentration: 17 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: = 68 % after 28 day
Result: readily biodegradable
Kinetic:

7 day	= 61 %
14 day	= 62 %
21 day	= 72 %

Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year: 1988 **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
Test condition: Direkteinwaage, da schlecht löslich

(29)

Type: aerobic
Inoculum: activated sludge
Concentration: 100 mg/l related to Test substance
Degradation: = 84 % after 14 day
Result: readily biodegradable
Method: other
Year: **GLP:** no data
Test substance: other TS
Source: MONTEFIBRE S.p.A. Milan
Test condition: OTHER TESTS - A Rhodococcus Sp. was grown on Seubert's mineral medium supplemented with 0.05% yeast extract and 0.2% DMT as sole carbon source, on a rotary shaker at room temperature (approx. 25°C). Stock cultures were maintained on mineral salts-dimethylterephthalate-agar slants. Growth of the bacterium was determined by measuring optical density at 660 nm in a photometer.

Test results: "The organism (Rhodococcus Sp.) degraded DMT by hydrolysis of ester-bonds to free terephthalic acid which in turn was metabolized through protocatechuate by an ortho-cleavage pathway. Methanol, the product of ester hydrolysis, also supported the growth of the organism. Thus the entire ester molecule was metabolized by Rhodococcus Sp.".
Test substance: DMT, no indication about purity.

(30) (31)

Type: aerobic
Inoculum: activated sludge, domestic
Concentration: 55 mg/l related to Test substance
Degradation: = 94 % after 28 day
Result: readily biodegradable
Method: other: BODIS Test (ISO Method 10708, in preparation)
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: degradation relates to oxygen comsumption
Source: Huels AG Marl

(32)

Type: aerobic
Inoculum: other bacteria: Rhodococcus sp., adaptiert
Concentration: 2 mg/l related to Test substance
Degradation: = 100 % after 2
Method: other: aerober Abbau im Batch-Test; Testsubstanz alleinige C-Quelle; UV-Analytik
Year: **GLP:** no data
Test substance: no data
Remark: Additional tests showed that dimethylterephthalat was obviously degraded by hydrolisis of ester-bonds to free terephthalic acid which was metabolized to protocatechuate by an ortho cleavage pathway
Source: Huels AG Marl

(33)

Type: aerobic
Inoculum: other bacteria: Pseudomonas acidovorans, adapted to Di-2-ethylhexylphthalate
Concentration: 6000 mg/l related to Test substance
Degradation: after 40 day
Result: under test conditions no biodegradation observed
Method: other: aerobic degradation in batch test; test substance was sole carbon source; parameters observed: Gas chromatography of test substance.
Year: **GLP:** no data
Test substance: no data
Remark: Bacteria isolated from soil and sewage; no statements concerning use of emulsifier (cf. water solubility!). No growth of inoculum after 40 days incubation.
Source: Huels AG Marl
Test condition: Incubation at 30 degree C, shaking

(34)

Type: aerobic
Inoculum: other bacteria: Rhodococcus erythropolis
Method: other: zitiert aus Abstract; keine Angaben zu Testbedingungen, Methode, Herkunft des Inokulums sowie Adaptation
Year: **GLP:** no data
Test substance: no data
Remark: Bioabbau in Boden:
Vollstaendiger Abbau einer Einsatzkonzentration von 250 mg/kg 10 Tage nach Inokulation;
Bioabbau in Abwasser:
Vollstaendiger Abbau von Dimethylterephthalat (keine Konzentrationsangabe) in belueftetem Abwasser nach 212-stuendiger Inkubation
Source: Huels AG Marl

(35)

3.6 BOD5, COD or BOD5/COD Ratio

C O D

Year: **GLP:** no
COD: = 60 mg/g substance

Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(29)

3.7 Bioaccumulation

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3.8 Additional Remarks

–

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: semistatic
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** yes
LC0: = 9.6
LC50: = 13
LC100: = 18
Method: other: Directive 92/69 EEC C 1
Year: 1992 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Source: Huels AG Marl

(36)

Type: static
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC0: = 10
LC50: = 18.8
LC100: = 25
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1988 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(37)

Type: static
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC0: = 10
LC50: = 18.8
LC100: = 25
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1988 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(37)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no
LC50: 69
Method: other: Bestimmung der Wirkung von Wasserinhaltsstoffen auf Fische, DIN 38412 Teil 15
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: Huels AG Marl

(38)

Type: static
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC50: = 14.3
Method: other
Year: **GLP:** no data
Test substance: other TS
Source: MONTEFIBRE S.p.A. Milan
Test substance: DMT, no indication about purity.

(39)

4.2 Acute Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC50 : = 30.4
Method: other
Year: **GLP:** no data
Test substance: other TS
Source: MONTEFIBRE S.p.A. Milan
Test substance: DMT,no indication about purity.

(40)

Species: Daphnia magna (Crustacea)
Exposure period: 24
Unit: mg/l **Analytical monitoring:** no
EC0: 6.8
EC50: > 26.5
Method: other: Daphnien-Kurzzeittest, DIN 38412 Teil 11, Bestimmung der Wirkung von Wasserinhaltsstoffen auf Kleinkrebse
Year: **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Source: Huels AG Marl

(41)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus subspicatus (Algae)
Endpoint: biomass
Exposure period: 72 hour(s)
Unit: mg/l **Analytical monitoring:** no
NOEC: = 10.8
EC50: = 27.6
Method: other
Year: **GLP:** yes
Test substance: other TS
Source: MONTEFIBRE S.p.A. Milan
Test substance: DMT, purity 99.99%.

(42)

Species: Scenedesmus subspicatus (Algae)
Endpoint:
Exposure period: 72
Unit: mg/l **Analytical monitoring:**
EC10: = 14.3
EC50: = 27.6
Method: other: Algenwachstumshemmtest nach Richtlinie 88/302/EWG
Year: 1984 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Ergebnis bezieht sich auf Zellwachstum
Source: Huels AG Marl

(43)

Species: Scenedesmus subspicatus (Algae)
Endpoint:
Exposure period: 72
Unit: mg/l **Analytical monitoring:**
EC10: = 20.1
Method: other: Algenwachstumshemmtest nach Richtlinie 88/302/EWG
Year: 1984 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Ergebnis bezieht sich auf Wachstumsrate
Source: Huels AG Marl

(43)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: activated sludge, domestic
Exposure period: 3 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC50: > 1000
EC20 : > 1000
EC80 : > 1000
Method: OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year: 1988 **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
Test condition: Direkteinwaage, da schlecht löslich

(29)

Type: aquatic
Species: Pseudomonas putida (Bacteria)
Exposure period: 5 hour(s)
Unit: mg/l **Analytical monitoring:** no
EC10: > 2000
Method: other: oxygen comsumption test (Huels method)
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Source: Huels AG Marl

(44)

Type:
Species: Pseudomonas putida (Bacteria)
Exposure period: 4 hour(s)
Unit: mg/l **Analytical monitoring:** no
EC10: > 2000
Method: other
Year: **GLP:** yes
Test substance: other TS
Remark: Test method: internal method of Huls AG.
Source: MONTEFIBRE S.p.A. Milan
Test substance: DMT, purity 99.99%.

(45)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

-

4.5.2 Chronic Toxicity to Aquatic Invertebrates

-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

-

4.6.2 Toxicity to Terrestrial Plants

-

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

-

4.7 Biological Effects Monitoring

Remark: Organism or ecosystem studied: Seawater - Algae: Phyllophora Nervosa, Acanthophora Delilei, Hypnea Musciformis.

Result: The compound isolated from algae was obtained as needles, mp 140°C; yield per Kg of algae: 0.075g for Phyllophora nervosa, 0.055g for Acanthophora delilei, 0.1g for Hypnea musciformis.
Comparision of the data related to the compound with those of an authentic sample showed that the compound was DMT.

Chemical analysis: Extraction with solvents (CHCl3 or MeOH or EtOAc) and separation of the evaporated residue onto a silica gel column. Eluition was carried out with Petrol-EtOAc (1:3). Eluates were collected and then evaporated. The residue was crystallized twicw from Et2O or Et2O-Petrol (1.4).

Comments: No data related to toxic effects in the Algae.

Source: MONTEFIBRE S.p.A. Milan
Test substance: See : "Test Results"

(46)

4.8 Biotransformation and Kinetics

-

4.9 Additional Remarks

Remark: Vorkommen in Rotalgen:
Phyllophora nervosa (Herkunft Schwarzes Meer) 75 mg/kg
Acanthophora delilei (Herkunft Mittelmeer, Aegaeis) 55 mg/kg
Hypnea musciformis (Herkunft Mittelmeer, Aegaeis) 100 mg/kg
Source: Huels AG Marl

(47)

Remark: Hydrolyse bei T = 25 Grad C und pH 7 mit einer Halbwertszeit von 46 Wochen
Source: Huels AG Marl

(48)

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type:	LD50		
Species:	rat		
Sex:			
Number of Animals:			
Vehicle:			
Value:	> 6590 mg/kg bw		
Method:	other		
Year:		**GLP:**	no data
Test substance:	other TS		
Source:	MONTEFIBRE S.p.A. Milan		
Test substance:	DMT (Eastman Organic Chemicals, Cat. N° 6580).		

(49)

Type:	LD50		
Species:	rat		
Sex:			
Number of Animals:			
Vehicle:			
Value:	3200 mg/kg bw		
Method:			
Year:		**GLP:**	no
Test substance:	no data		
Source:	Huels AG Marl		

(50)

Type:	LD50		
Species:	rat		
Sex:			
Number of Animals:			
Vehicle:			
Value:	4390 mg/kg bw		
Method:			
Year:		**GLP:**	no
Test substance:	no data		
Source:	Huels AG Marl		

(51)

Type:	LD50		
Species:	rat		
Sex:			
Number of Animals:			
Vehicle:			
Value:	> 6590 mg/kg bw		
Method:	other: see reference		
Year:	1973	**GLP:**	no
Test substance:	no data		
Source:	Huels AG Marl		

(52)

date: 18-FEB-2000

5. Toxicity Substance ID: 120-61-6

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: > 4600 mg/kg bw
Method:
Year: **GLP:** no
Test substance: no data
Source: Huels AG Marl

(53)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: > 10000 mg/kg bw
Method:
Year: **GLP:** no
Test substance: no data
Source: Huels AG Marl

(54)

Type: LD100
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: 4500 mg/kg bw
Method:
Year: **GLP:** no
Test substance: no data
Source: Huels AG Marl

(55)

Type:
Species:
Sex:
Number of Animals:
Vehicle:
Value:
Method:
Year: **GLP:**
Test substance:
Remark: Después de alimentar ratas con dietas que contenían 0.25%, 0.50%, ó 1.0% de Dmt, durante 96 días, no se informó de hallazgos biológican¡mente significativos.
LD50 oral aguda- >6590 mg/kg (ratas)
>3200 mg/kg (ratones).
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value: > 6 mg/l
Method: other
Year: **GLP:** no data
Test substance: other TS
Source: MONTEFIBRE S.p.A. Milan
Test substance: DMT, no indication about purity.

(56)

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: guinea pig
Sex:
Number of Animals:
Vehicle:
Value: > 5000 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: other TS
Source: MONTEFIBRE S.p.A. Milan
Test substance: DMT, no indication about purity.

(57)

Type: LD50
Species: guinea pig
Sex:
Number of Animals:
Vehicle:
Value: > 5000 mg/kg bw
Method:
Year: **GLP:** no data
Test substance: no data
Source: Huels AG Marl

(50)

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: > 3200 mg/kg bw
Method:
Year: **GLP:** no data
Test substance: no data
Source: Huels AG Marl

(50)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: 3900 mg/kg bw
Method: other: see reference
Year: 1973 **GLP:** no
Test substance: no data
Remark: Symptoms: weakness, slight tremors, ataxia; all deaths occurring within 48 hours after injection
Source: Huels AG Marl

(52)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: 3650 mg/kg bw
Method:
Year: **GLP:** no
Test substance: no data
Source: Huels AG Marl

(53)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: 3000 mg/kg bw
Method:
Year: **GLP:** no
Test substance: no data
Source: Huels AG Marl

(54)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: slightly irritating
EC classificat.: not irritating
Method: other
Year: **GLP:** no data
Test substance: other TS
Source: MONTEFIBRE S.p.A. Milan
Test substance: DMT, no indication about purity.

(58)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.:
Method: other: see RM
Year: **GLP:** no data
Test substance: no data
Remark: a semiocclusive application (20 h) of a 50 % suspension with aqua dest. was not irritating on the depilated skin of albino rabbits;
Source: Huels AG Marl

(54)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.:
Method: other: US EPA and TSCA Guideline "Primary Dermal Irritation"
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: irritation index: 0.0/8
Source: Huels AG Marl

(59)

Species: guinea pig
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.:
Method: other: see reference
Year: 1973 **GLP:** no
Test substance: no data
Remark: 0.5 ml of a 1 % solution (acetone:dioxane:guinea pig fat - 7:2:1) was dropped on the depilated skin;
up to 4 applications;
no irritation was observed;
Source: Huels AG Marl

(52)

Species: guinea pig
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result:
EC classificat.:
Method:
Year: **GLP:** no data
Test substance: no data
Remark: method: 5 g/kg (in aqua dest.), application for 24 h under occlusion, slight irritation reactions were observed;
not classifiable according to current EEC directives;
Source: Huels AG Marl

(60)

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: slightly irritating
EC classificat.: not irritating
Method: other
Year: **GLP:** no data
Test substance: other TS
Source: MONTEFIBRE S.p.A. Milan
Test substance: DMT, no indication about purity.

(61)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result:
EC classificat.:
Method:
Year: **GLP:** no
Test substance: no data
Remark: Application of 2 drops of a suspension of 5 % substance in starch caused irritation of the mucous membranes of the eyes. No further details reported.
Not classifiable according to current EEC directives.
Source: Huels AG Marl

(62)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result:
EC classificat.:
Method:
Year: **GLP:** no data
Test substance: no data
Remark: Application of 500 mg to the eyes for 24 h produced moderate irritation. No further details reported.
Not classifiable according to current EEC directives.
Source: Huels AG Marl

(63)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result:
EC classificat.:
Method:
Year: **GLP:** no
Test substance: no data
Remark: Only slight redness (lasting for a few hours) was observed after application of 0.05 g test substance (powder) into the conjunctival sac of the eye. No further details reported. Not classifiable according to current EEC directives.
Source: Huels AG Marl

(54)

Species: guinea pig
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: not irritating
EC classificat.:
Method:
Year: **GLP:** no
Test substance: no data
Remark: No irritation was observed after application of a 15 % solution in oil. No further details reported. Not classifiable according to current EEC directives.
Source: Huels AG Marl

(53)

5.3 Sensitization

Type: other
Species: guinea pig
Number of Animals:
Vehicle:
Result: not sensitizing
Classification: not sensitizing
Method: other
Year: **GLP:** no data
Test substance: other TS
Source: MONTEFIBRE S.p.A. Milan
Test substance: DMT. no indication about purity.

(64)

Type:
Species: guinea pig
Number of Animals:
Vehicle:
Result: not sensitizing
Classification:
Method:
Year: **GLP:** no
Test substance: no data
Remark: "Drop on" technique: 0.5 ml of a 1 % solution of test substance in acetone, dioxane and guinea-pig fat (7:2:1) was dropped on the rump areas of 10 guinea pigs; 24 and 48 hours later these areas were observed for primary irritation. After 3 additional applications of this solution in the next 5 days and a 3 week rest period, challenging doses were applied to the right shoulder and a week later to the left shoulder areas.
"footpad" technique: 10 animals were treated as in the "drop on" technique for primary irritation; 1 week later, the compound solution was mixed with whole heparinized rabbit blood (1.0 %) for 1 - 3 hours and 0.05 ml of this mixture was injected into a footpad; 1 week later, the skin was challanged with a drop of the substance solution.
No senstization was observed.
Not classifiable according to current EEC directives.
Source: Huels AG Marl

(52)

5.4 Repeated Dose Toxicity

Species: rat **Sex:** no data
Strain: no data
Route of admin.: inhalation
Exposure period: 5 months
Frequency of treatment: 2 h/day
Post. obs. period:
Doses: 40 - 70 mg/m3 (vapors and aerosol)
Control Group:
Method:
Year: **GLP:** no
Test substance: no data
Result: Death of 30 % of the animals in 10 - 12 weeks from disorders of the blood and lymph circulation; In animals sacrificed a diffuse respiratory inflammatory process and emphysema were observed. Also distrophic changes of the liver and the kidneys, rhinitis, and tracheitis were observed.
No further details reported.
Source: Huels AG Marl

(62)

Species: rat **Sex:** male
Strain: Sprague-Dawley
Route of admin.: inhalation
Exposure period: 24 weeks
Frequency of treatment: 6 h/day, 5 days/week
Post. obs. period:
Doses: 0.015 mg/l
Control Group:
Method:
Year: **GLP:** no data
Test substance: no data
Result: No detectable effects on body weights, organ weights, or routine clinical chemistry or urinalysis parameters were observed. Gross and histopathologic evaluations of tissues from treated animals were within normal limits.
Source: Huels AG Marl

(65)

Species: rat **Sex:** male
Strain: Long-Evans
Route of admin.: inhalation
Exposure period: 58 exposures
Frequency of treatment: 4 h/day, 5 days/week
Post. obs. period: 24, 48 weeks
Doses: "dust clouds" containing 0.0165, 0.0864 mg/l
Control Group: yes
Method:
Year: **GLP:** no
Test substance: no data
Remark: 30 rats/group
The percentage of respirable particles (</= 5 um) was 36 %, the calculated average daily doses were 0.7 and 4.0 mg/kg.
Result: the high concentration caused nose rubbing, preening and blinking; weight gain, hematologic and clinical chemistry, liver and kidney weights, and histopathologic parameters were similar in treated and control animals; follow-up hematology, blood chemistry and pathology examinations on the rats at 24 and 48 weeks post-exposure showed no latent changes
Source: Huels AG Marl

(52)

Species: rat **Sex:** no data
Strain: no data
Route of admin.: inhalation
Exposure period: 5 months
Frequency of treatment: 2 h/day
Post. obs. period:
Doses: 1 - 4 mg/m3 (vapors and aerosol)
Control Group:
Method:
Year: **GLP:** no
Test substance: no data
Result: Inhibition of nervous system functions, slight anemia, reticulocytosis, hypertonia; chronic inflammation was found in a morphological study of the respiratory organs; no further details reported;
Source: Huels AG Marl

(62)

Species: rat **Sex:** male/female
Strain: Wistar
Route of admin.: oral feed
Exposure period: 13 weeks
Frequency of treatment: continuously in diet
Post. obs. period:
Doses: 0.5, 1.6, 3 % in the diet
Control Group:
Method:
Year: **GLP:** no data
Test substance: no data
Result: Dimethyl terephthalate induced bladder calculi in high dosed males (12/16) and females (6/16), middle dosed males (1/19) and low dosed males (2/19). Mild to moderate hyperplasia of the bladder urothelium was diagnosed in 11/16 males and 7/16 females of the high dosed group. Pathologic effects due to treatment were limited to the kidney and the bladder. There was no evidence of neoplastic change. A strong correlation was found between the presence of uroliths and the development of bladder hyperplasia: in the high dosed group 100 % (11/11) males and 86 % (6/7) females with hyperplasia had bladder stones.
Source: Huels AG Marl

(66)

Species: rat **Sex:** male/female
Strain: Fischer 344
Route of admin.: oral feed
Exposure period: 13 weeks
Frequency of treatment: continuously in diet
Post. obs. period: none
Doses: 1750, 2500, 5000, 10000, 20000 ppm
Control Group: yes
NOAEL: = 5000 ppm
Method:
Year: **GLP:** no data
Test substance: other TS: technical grade
Remark: 10 animals/sex/dose
Result: No compound-related effects were noted in the physical appearance, behaviour, or food consumption of the rats. All rats survived until the end of the study. Body weight gains were reduced in the two high dose groups of both sexes. No gross alterations related to the chemical were noted in the dosed rats at necropsy. Microscopically diffuse hepatic cell swelling in the livers was observed in rats from all dosed groups. This finding was considered to be compound related but not dose related.
Source: Huels AG Marl

(67)

Species: rat **Sex:** male
Strain: Long-Evans
Route of admin.: oral feed
Exposure period: 96 d
Frequency of treatment: continuously in diet
Post. obs. period: 24, 48 weeks
Doses: 0.25, 0.5, 1.0 %
Control Group: yes
NOAEL: = .5 %
Method:
Year: **GLP:** no
Test substance: no data
Remark: 30 weanling male rats/group
Result: Reduced body weight gain was observed in the high dose group. Food consumption, hematologic and clinical chemistry, liver and kidney weight and histopathologic parameters were similar in treated and control animals. Follow-up hematology, blood chemistry and pathology examinations on the rats at 24 and 48 weeks post-exposure showed no latent changes.
Source: Huels AG Marl

(52)

Species: rat **Sex:** no data
Strain: no data
Route of admin.: unspecified
Exposure period: 39 day
Frequency of treatment: day
Post. obs. period:
Doses: 500mg/Kg/day
Control Group: no data specified
NOAEL: = 500 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: other TS
Source: MONTEFIBRE S.p.A. Milan
Test substance: DMT, no indication about purity.

(68)

Species: rat **Sex:**
Strain:
Route of admin.: oral unspecified
Exposure period: 2 weeks
Frequency of treatment: 5 d/week
Post. obs. period:
Doses: 5000 mg/kg
Control Group:
Method:
Year: **GLP:** no data
Test substance: no data
Result: Transient discomfort and progressive weight loss during the treatment. 5/6 animals died with pathology suggestive of starvation.
No further details reported.
Source: Huels AG Marl

(69)

Species: rat **Sex:** female
Strain:
Route of admin.: i.p.
Exposure period: 109 days
Frequency of treatment: injection every 7. day
Post. obs. period:
Doses: 1 - 1.7 ml/animal (15% suspension in olive oil), total dose: 3.5 g/animal
Control Group: yes, concurrent vehicle
Method:
Year: **GLP:** no data
Test substance: no data
Remark: 10 female rats (strain not specified) received 1 - 1.7 ml of a 15 % suspension of the test substance in olive oil by i.p. injection once a week for 109 days (total dose: 3.5 g/animal).
Result: Retardation of body weight gain was observed, starting after 6 weeks. 1 rat died after 56 days. No histopathological findings were observed.
No further details reported.
Source: Huels AG Marl

(53)

Species: mouse **Sex:** male/female
Strain: B6C3F1
Route of admin.: oral feed
Exposure period: 13 weeks
Frequency of treatment: continuously in diet
Post. obs. period:
Doses: 1750, 2500, 5000, 10000, 20000 ppm
Control Group: yes
Method:
Year: **GLP:** no data
Test substance: other TS: technical grade
Remark: 10 animals/sex/dose
Result: No compound-related effects were noted in the physical appearance, behavior, or food consumption of the mice. One male each at 2500, 5000 and 20000 ppm and two females at 20000 ppm died. No distinct effects of the test chemical on body weight gain were observed at any dose.
No gross alterations related to the test chemical were noted in the dosed mice at necropsy. Microscopically diffuse hepatic cell swelling in the livers was observed in all dosed groups. This finding was considered to be compound related but not dose related.
Source: Huels AG Marl

(67)

Species: dog **Sex:** no data
Strain: no data
Route of admin.: oral unspecified
Exposure period: up to 62 days
Frequency of treatment:
Post. obs. period:
Doses: 100 mg/kg/day (40 days), 200 mg/kg/day (62 days)
Control Group:
Method:
Year: **GLP:** no data
Test substance: no data
Result: Increased irritability in 2/4 animals. Downward trend in systolic and diastolic pressure in 3/4 animals. No gross or microscopic pathologic changes were observed.
No further details reported.
Source: Huels AG Marl

(69)

Species: guinea pig **Sex:** male
Strain: Hartley
Route of admin.: inhalation
Exposure period: 24 weeks
Frequency of treatment: 6 h/day, 5 days/week
Post. obs. period:
Doses: 0.015 mg/l
Control Group:
Method:
Year: **GLP:** no data
Test substance: no data
Result: No detectable effects on body weights, organ weights, or routine clinical chemistry or urinalysis parameters were observed. Gross and histopathologic evaluations of tissues from treated animals were within normal limits.
No further details reported.
Source: Huels AG Marl

(65)

Species: pig **Sex:**
Strain:
Route of admin.: oral feed
Exposure period: 30 days
Frequency of treatment: continuously in diet
Post. obs. period:
Doses: 2, 260 mg/kg and one higher dose (not specified)
Control Group:
Method:
Year: **GLP:** no data
Test substance: no data
Remark: 5 pigs/group, age: 2-4 months
Result: In the two high dose groups, retardation of body weight gain, restlessness, scratching, diarrhea, variation of the numbers of leucocytes, and increase of immuneglobulines, indicating an immunity reaction were observed. At necroscopy gastroenteritis, inflammation of bronchi and lungs and circumscribed changes in livers and kidneys were observed. Traces of the test substance were found in the stomach, the intestine, the muscle tissues, the liver, the kidneys and the skin.
Source: Huels AG Marl

(70)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Concentration:
Metabolic activation: with and without
Result: negative
Method: Directive 84/449/EEC, B.14 "Other effects - Mutagenicity (Salmonella typhimurium - reverse mutation assay)"
Year: 1984 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Spot-test
Source: Huels AG Marl

(71)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 102, TA 1535, TA 1537, TA 1538
Concentration: up to 5000 æg/plate
Metabolic activation: with and without
Result: negative
Method: other: according to Ames et al., Mutat. Res. 31, 347-364
Year: 1975 **GLP:** no data
Test substance: no data
Remark: solvent: mixture of DMSO and Tween 20 (29:1)
Source: Huels AG Marl

(72)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration: up to 333.3 æg/plate
Metabolic activation: with and without
Result: negative
Method: other: according to Ames et al., Mutat.Res. 31, 347-364
Year: 1975 **GLP:** no data
Test substance: other TS: purity 99%
Remark: solvent: DMSO
preincubation assay
Source: Huels AG Marl

(73) (74)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration: no data
Metabolic activation: with and without
Result: negative
Method: other: according to Ames et al., Mutat.Res. 31, 347-364
Year: 1975 **GLP:** no data
Test substance: no data
Source: Huels AG Marl

(75)

Type: Cytogenetic assay
System of testing: Chinese hamster ovary cells
Concentration: up to 10æg/ml
Metabolic activation: with and without
Result: negative
Method:
Year: **GLP:** no data
Test substance: other TS: purity 99%
Source: Huels AG Marl

(76)

Type: Cytogenetic assay
System of testing: human peripheral blood lymphocytes
Concentration: up to 500 æg/ml
Metabolic activation: without
Result: negative
Method:
Year: **GLP:** no data
Test substance: other TS: purity 99%
Source: Huels AG Marl

(72)

Type: Mouse lymphoma assay
System of testing: L5178Y mouse lymphoma cells clone 3.7.2C
Concentration: up to 100 æg/ml
Metabolic activation: with and without
Result: negative
Method:
Year: **GLP:** no data
Test substance: no data
Source: Huels AG Marl

(77)

Type: Sister chromatid exchange assay
System of testing: Chinese hamster ovary cells
Concentration: up to 10 æg/ml
Metabolic activation: with and without
Result: negative
Method:
Year: **GLP:** no data
Test substance: other TS: purity 99%
Source: Huels AG Marl

(76)

Type: Unscheduled DNA synthesis
System of testing: Hela cells
Concentration: up to 5000 æg/ml
Metabolic activation: with and without
Result: negative
Method:
Year: **GLP:** no data
Test substance: other TS: purity 99%
Source: Huels AG Marl

(72)

Type: other: Bioluminescence assay
System of testing: Photobacterium phosphoreum
Concentration: no data
Metabolic activation:
Result: ambiguous
Method:
Year: **GLP:** no data
Test substance: no data
Remark: The test utilizes dark mutants of a Photobacterium strain that have lost the ability to produce light presumably by the repression of the luminescence operon. The ability of chemicals to restore luminescence, probably by depression of the luminescence operon, is tested.
No further details reported.
Source: Huels AG Marl

(78)

Type: other: DNA single-strand breaks
System of testing: primary rat hepatocytes
Concentration: up to 15 æmol/tube
Metabolic activation: without
Result: negative
Method:
Year: **GLP:** no data
Test substance: other TS: purity 99%
Source: Huels AG Marl

(72)

Type: other: DNA single-strand breaks
System of testing: SV40-transformed Chinese hamster embryo cells (CO60 line)
Concentration: no data
Metabolic activation: without
Result: negative
Method:
Year: **GLP:** no data
Test substance: other TS: purity 99%
Source: Huels AG Marl

(72)

Type: other: Micronucleus test
System of testing: human peripheral blood lymphocytes
Concentration: up to 500 æg/ml
Metabolic activation: without
Result: negative
Method:
Year: **GLP:** no data
Test substance: other TS: purity 99%
Source: Huels AG Marl

(72)

Type: other: Selective DNA amplification
System of testing: AAV2-infected Syrian hamster embryo cells
Concentration: up to 10 æg/ml
Metabolic activation: without
Result: negative
Method:
Year: **GLP:** no data
Test substance: other TS: purity 99%
Source: Huels AG Marl

(72)

Type: other
System of testing: DNA SINGLE-STRAND BREAKS IN PRIMARY HEPATOCYTES.
Concentration:
Metabolic activation: no data
Result: negative
Method: other
Year: **GLP:** no data
Test substance: other TS
Remark: Dmt did not produce DNA damage in primary rat hepatocytes, and did not produce chromosome aberration in human lymphocytes.
Source: MONTEFIBRE S.p.A. Milan
Test substance: Dmt, no indication about purity.

(79)

5.6 Genetic Toxicity 'in Vivo'

Type: Dominant lethal assay
Species: Drosophila melanogaster **Sex:** male
Strain:
Route of admin.: oral feed
Exposure period:
Doses:
Result:
Method:
Year: **GLP:** no data
Test substance: no data
Result: An increased frequency of dominant lethal mutations was observed in males.
concentration of test substance in agar: 150 mM.
No further details reported.
Source: Huels AG Marl

(80)

Type: Micronucleus assay
Species: mouse **Sex:** male
Strain: other: (C57BI/6jxCBA)F1
Route of admin.: i.p.
Exposure period: single injection
Doses: 0.2, 0.25, 0.33, 0.5, and 1.0 mmol/kg
Result:
Method:
Year: **GLP:** no data
Test substance: other TS: purity 99.9%
Remark: 15 mice/group
Mice were sacrificed 24, 48 and 72 h after injection.
Result: All concentrations tested significantly increased the micronucleus frequency in bone marrow polychromatic erythrocytes, the maximum effect being obtained 24 h after treatment. The micronucleus frequency decreases to the control level at the later sample times.
Source: Huels AG Marl

(81)

Type: other
Species: Drosophila melanogaster **Sex:** no data
Strain: no data
Route of admin.: unspecified
Exposure period:
Doses:
Result:
Method: other
Year: **GLP:** no data
Test substance: other TS
Remark: The effect of DMT on the frequency of dominant lethal mutations in Drosophila sex cells has been studied. DMT induced mutations in both imagos and developing Drosophila.
Source: MONTEFIBRE S.p.A. Milan
Test substance: DMT, no indication about purity.

(82)

5.7 Carcinogenicity

Species: rat **Sex:** male/female
Strain: Fischer 344
Route of admin.: oral feed
Exposure period: 103 weeks
Frequency of treatment: continuously in diet
Post. obs. period: 2 weeks
Doses: 2500, 5000 ppm
Result:
Control Group: yes
Method:
Year: **GLP:** no data
Test substance: other TS: technical grade
Remark: 50 male and 50 female rats/group
The test substance was administered in a diet containing 2 % corn oil. The control animals received only 2 % corn oil in the diet.
Result: Administration of dimethyl terephthalate had no appreciable effect on mean body weights of either sex. No treatment related clinical signs were observed.
Degenerative, proliferative and inflammatory lesions were similar in number and kind to those commonly found in aged F344 rats.
In the male and female rats, no tumours occurred in dosed groups at incidences that were significantly higher than those for corresponding control groups.
Although rats may not have received a dose of the test chemical sufficiently high to provide maximum test sensitivity, it is concluded that under the conditions of this bioassay, dimethyl terephthalate was not carcinogenic.
Source: Huels AG Marl

(67)

Species: mouse **Sex:** male/female
Strain: B6C3F1
Route of admin.: oral feed
Exposure period: 103 weeks
Frequency of treatment: continuously in diet
Post. obs. period: 2 weeks
Doses: 2500, 5000 ppm
Result:
Control Group: yes
Method:
Year: **GLP:** no data
Test substance: other TS: technical grade
Remark: 50 male and 50 female mice/group
The test substance was administered in a diet containing 2 % corn oil. The control animals received only 2 % corn oil in the diet.
Result: Administration of dimethyl terephthalate had no appreciable effect on mean body weights of either sex.
Except for higher incidences of alopecia among dosed female

mice and injuries due to fighting among dosed male mice, clinical signs were associated with aging and were common to both dosed and control groups.
In the male mice, alveolar/bronchiolar adenomas or carcinomas occurred at incidences that were dose related, and in direct comparisons the incidences were significantly higher in the dosed groups than that in the matched-control group. The incidences of alveolar/bronchiolar adenomas or carcinomas and their variability in three other concurrent control groups of B6C3F1 mice did not permit the conclusion that the incidence of these tumors observed in dosed male mice in this study was associated with the administration of the test chemical.
In the female mice, lymphomas occurred at incidences that were dose related. However, there was a departure from linear trend, because the incidence in the control group was higher than that in the low-dose group. The occurrence of lymphomas in the dosed females cannot clearly be related to the administration of the test chemical.
Although mice may not have received a dose of the test chemical sufficiently high to provide maximum test sensitivity, it is concluded that under the conditions of this bioassay, there is no evidence of carcinogenic activity of dimethyl terephthalate in female mice and equivocal evidence of carcinogenic activity in male mice.

Source: Huels AG Marl

(67)

Species: rat **Sex:** male/female
Strain: no data
Route of admin.: other
Exposure period: 103 weeks
Frequency of treatment:
Post. obs. period: 2 weeks
Doses: 2500 or 5000ppm of DMT
Result:
Control Group: yes, concurrent no treatment
Method: other
Year: **GLP:** no data
Test substance: other TS
Remark: TEST RESULTS: "There were no appreciable effects on body weights, clinical signs, or survival. Both species may have been able to tolerate higher doses. DMT did not produce an increased incidence of tumors among male or female rats or among female mice. The incidence of lung tumors in the male mice (27%) administered the high dose of DMT appeared to be significantly increased when compared with the concurrent control group. Because the lung tumor incidence in this control group was unusually low, pooled results from three other control groups were compared. In this pooled group, lung tumor incidence was between 10 and 18%. In its final analysis of these data, NCI concluded the data do not provide clear evidence regarding the carcinogenic potential of DMT".
Source: MONTEFIBRE S.p.A. Milan

Test substance: DMT, no indication about purity.

(83)

5.8 Toxicity to Reproduction

Type: Fertility
Species: rat **Sex:** male/female
Strain: Long-Evans
Route of admin.: oral feed
Exposure Period: see RM
Frequency of treatment: continuously in diet
Premating Exposure Period
male: 115 days
female: 6 days
Duration of test:
Doses: 0.25, 0.5, 1.0 % in the diet
Control Group: yes
Method:
Year: **GLP:** no
Test substance: no data
Remark: When paired the males had been on the experimental diet for 115 days and the females for 6 days. Both sexes ingested the compound during the week of mating, then the males received control diet and the females remained on experimental diet throughout the periods of gestation, parturition and lactation.
Result: No adverse effect on libido, pregnancy, gestation, litter size and viability of the young rats were observed. The pups born to parents fed 0.5 and 1 % diet had significantly (p </= 0.05) lower average body weights at weaning when compared to the controls.
Source: Huels AG Marl

(52)

Type: One generation study
Species: rat **Sex:** male
Strain: Long-Evans
Route of admin.: oral feed
Exposure Period: 115 days
Frequency of treatment:
Premating Exposure Period
male: 115 days
Duration of test:
Doses: 0.25, 0.50, 1% of DMT.
Control Group: no data specified
NOAEL Parental: = 1 %
NOAEL F1 Offspr.: = .25 %
Method: other
Year: **GLP:** no data
Test substance: other TS
Remark: TEST RESULTS: "No effects were observed on fertility, reproductive capacity, libido, pregnancy, gestation, litter size or the viability of the young. The pups born to parents fed 0.5 and 1.0% DMT had significantly lower average body

weights at weaning when compared to the controls".
Source: MONTEFIBRE S.p.A. Milan
Test substance: DMT (Eastman Organic Chemicals, Cat. N° 6580).

(84)

5.9 Developmental Toxicity/Teratogenicity

Species: rat **Sex:** no data
Strain: no data
Route of admin.: inhalation
Exposure period:
Frequency of treatment:
Duration of test:
Doses: 1mg/m3 of DMT
Control Group:
Method: other
Year: **GLP:** no data
Test substance: other TS
Remark: TEST METHOD: INHALATION "Thirty pregnant rats were exposed to 1 mg/m3 of DMT throughout gestation"
Result: TEST RESULTS: "No abnormal developmental effects and no pre- or post-implantation losses were noted".
Source: MONTEFIBRE S.p.A. Milan
Test substance: DMT, no indication about purity.

(85)

Species: rat **Sex:** female
Strain: no data
Route of admin.: inhalation
Exposure period: throughout gestation (20 days)
Frequency of treatment: 24 hours/day
Duration of test:
Doses: 1 mg/m3
Control Group: yes
Method:
Year: **GLP:** no
Test substance: no data
Remark: dose group: 30 rats
control group: 17 rats
Result: Maternal toxic effects but no embryotoxicity or teratogenicity were reported.
No further details reported.
Source: Huels AG Marl

(86)

Species: rat **Sex:** female
Strain: Wistar
Route of admin.: gavage
Exposure period: gestation day 7 - 16
Frequency of treatment: once daily
Duration of test:
Doses: 1000 mg/kg
Control Group: yes, concurrent vehicle
Method:
Year: **GLP:** no data
Test substance: no data
Result: No maternal toxicity and no embryotoxic or teratogenic effects were observed.
Source: Huels AG Marl

(87)

Species: rat **Sex:** female
Strain:
Route of admin.: gavage
Exposure period: 7.- 16. Graviditätsta
Frequency of treatment: täglich
Duration of test:
Doses: 1000 mg/kg Kgw.
Control Group: yes, concurrent vehicle
NOAEL Maternalt.: > 1000 mg/kg bw
Method: OECD Guide-line 414 "Teratogenicity"
Year: 1986 **GLP:** yes
Test substance: no data
Remark: Vehikel: Stärkeschleim
Result: Ergebnis: Keine Beeinträchtigung des allgemeinen Gesundheitszustands der Muttertiere. Die Feten waren normal entwickelt und wiesen keine Anomalien auf.
No effect: maternal, embryonal, fetalen Toxizität = 1000 mg/kg Kgw.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(88)

5.10 Other Relevant Information

Type: Biochemical or cellular interactions
Remark: Urolithiasis was induced in weaning Fischer-344 rats by feeding a diet containing 0.5 - 3 % dimethylterephthalate (DMT) within 2 weeks. 28 days old pups were removed from their dams, dosed for 2 weeks and sacrificed on the last day of treatment. Calculus formation seemed to be dose and sex dependent. Extremely steep dose-response curves were found in males and females spanning the dietary concentration range of 1.5 - 3 %. Uroliths were detected in 100 % of the males (18/18) and in 46.7 % of the females (7/15) at the highest dose. Aciduria and hypercalciuria were associated with the development of calculi containing primarily Ca-TPA. In principle chemical stone composition was identical in rats treated with terephthalic acid (TPA)

or DMT. Histological investigations were limited to TPA treated rats. Hyperplasia of the transitional epithelium (micropapillae) and invasive growth was found only in animals with bladder stones. These results indicated that critical saturating concentrations of TPA and calcium are necessary for stone development. Pathological epithelial changes were described as a result of multiple stone formation and not as a direct cause of DMT-treatment.

Source: Huels AG Marl

(89) (90)

Type: Toxicokinetics

Remark: When rats were fed diets containing 5% DMT for five days, the compound was almost completely absorbed and eliminated by the kidney. Only a trace of the indigest ester that is absorbed is excreted unchanged in the urine; the rest is metabolized to TPA. About 15% of the unabsorbed ester appears in the feces; the balance is probably also destroyed by the intestinal flora.

Source: MONTEFIBRE S.p.A. Milan

(91)

Type: Toxicokinetics

Remark: Female F-344 rats received 1 or 2 % dimethylterephthalate in diet for 3 weeks.
The urine of the rats was collected and examined. The treatment with dimethylterephthalate resulted in specific changes in urinary ions, including hypercalciuria and urinary acidosis.
Terephthalic acid was detected in the urine, whereas the parent compound was not found.
The results indicate that metabolism of the substance to terephthalic acid occurs extensively in rats, and accounts for the ion changes observed in this study.
Three male rats were dosed once orally with suspensions of 14C-labelled substance. Urine and feces were collected for 24 hours. Only 14C-terephthalic acid was detected in the urine samples. Treatment of urine with glucuronidase and aryl sulfatase did not change the appearance of the radiochromatograms. In the feces, trace amounts of monomethyl 14C-terephthalic acid and of the parent compound were detected.
Approximately 86% of the administered radioactivity was eliminated via urine following a single oral dose. In agreement with this, analysis of fecal samples showed very little radioactivity, and only trace levels of radioactivity were found in the carcass after 48 hr.
In contrast, the major metabolite found in the urine of B6C3F1 mice after oral dosing of 14C-dimethyl- terephthalate was monomethyl-14C-terephthalate, indicating a minor capacity to hydrolyse the test substance.

Source: Huels AG Marl

(92) (93)

Type: Toxicokinetics
Remark: Rats received 5 % dimethylterephthalate in diet for 5 days. The compound was almost completely absorbed and eliminated by the kidney. Only a trace of absorbed substance is excreted unchanged in the urine, the major part is metabolized to terephthalic acid. About 15 % of the unabsorbed substance appears in the feces.
Source: Huels AG Marl

(94)

Type: Toxicokinetics
Remark: Data from a tracer study in rabbits and rats to determine the absorption, distributionm and excretion of terephthtalic acid (TA) and deimethyl terephthtalate (DMT) following oral, intratracheal, dermal and ocular administration indicate:
1) a rapid absorption and excretion of 14C-TA and 14C-DMT with no evidence of tissue accumulation in rats following single or repeated oral and intratracheal administration
2) recovery of approximately 11% of a single dose and 13% of five repeated cutaneous doses of 14C-DMT from the urine and feces of rats within 10 days after initial dosing
3) no significant absorption of 14C-TA when applied to the conjunctival sac of one eye of eight rabbits
4) excretion of approximately 33% of a single ocular dose (50 mg) of 14C-DMT in the urine and feces of rabbits within 10 days after instillation with no evidence of tissue accumulation or ocular damage.
These results suggest that TA and DMT are rapidly absorbed and excreted and that no significant quantities of these compounds accumulate in the tissues following single or repeated oral, intratracheal, dermal, or ocular administration to laboratory animals.
Source: Huels AG Marl

(95)

5.11 Experience with Human Exposure

Remark: One russian study reports no adverse effects in workers exposed to hight concentration of DMT.
Source: MONTEFIBRE S.p.A. Milan

(96)

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7.1 Risk Assessment

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SECTION 2.

ISOPHTHALIC ACID (CAS RN 121-91-5)

OECD SIDS SUBMISSIONS (SIAP AND SIAR DOSSIER) FOR ISOPHTHALIC ACID (CAS RN 121-91-5)

FOREWORD INTRODUCTION

ISOPHTHALIC ACID

CAS N°: 121-91-5

SIDS Initial Assessment Report for 14th SIAM

(Paris, France, March 2002)

Chemical Name: ISOPHTHALIC ACID

CAS No: 121-91-5

Sponsor Country: United States of America / ICCA

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HISTORY: Documents were prepared and reviewed by industry prior to submission to sponsor country. Sponsor country conducted reviews of submitted data and offered comments to industry. Industry prepared and resubmitted documents for consideration at SIAM 14. Literature searches were conducted on Medline, PubMed, and Toxline. The following database sources were reviewed: Hazardous Substances Data Bank (HSDB); SRI 2000 Chemical Economics Handbook; SRC PhysProp Database; Registry of Toxic Effects of Chemical Substances; IUCLID Data Sheet; International Chemical Safety Cards; NIOSH Summary; International Occupational Safety and Health Information Centre; NTP Chemical Repository;

Testing: **No testing** **(X)**

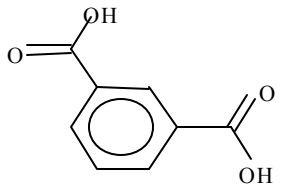
Testing **( )**

COMMENTS:

Deadline for circulation: February 1, 2002

Date of Circulation:

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	121-91-5
Chemical Name	Isophthalic acid
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Category/Analogue Rationale

For most SIDS endpoints, adequate data are available for isophthalic acid (IPA) to provide a characterization of its toxicity. Due to not having sufficient data for the endpoints of reproductive toxicity and *in vivo* genotoxicity with IPA, information on terephthalic acid (or TPA, CAS No. 100-21-0), an isomer of IPA was used as a surrogate. IPA and TPA are structural isomers, with carboxylic acid groups on the benzene ring at 1,3- and 1,4-carbons, respectively. Both IPA and TPA have similar physicochemical properties and show similar metabolic pathways and toxicological properties.

Human Health

In rats, both IPA and TPA are eliminated from the body unchanged primarily via urinary excretion. A steady state in blood is achieved fairly rapidly after inhalation exposure (on the first day) to IPA. One week after cessation of exposure, IPA was no longer detectable in the blood. Based on the Log Kow (2.34), IPA is not expected to accumulate appreciably in tissues and is likely to be readily excreted from the body.

IPA exhibits low acute toxicity by the oral, dermal, and inhalation routes. The oral LD50 has been reported from >5000 mg/kg (no deaths) to 13,000 mg/kg in rats. No mortality was observed in rats following acute inhalation exposures to 11,400 mg/m^3 or acute dermal doses in rabbits of 23,000 mg/kg. IPA is not a skin sensitizer as skin reactions were only seen in 10% of the animals. IPA has negligible skin irritation potential and was considered slightly irritating to the eyes.

In repeated dose studies, the target organ is the kidney. A NOAEL of 250 mg/kg-day for IPA for kidney effects (crystalluria, mild hydronephrosis, pelvic calcification) has been reported for rats following repeated oral exposures. No systemic effects were observed in rats following repeated inhalation exposures to 10 mg/m^3 of IPA. Evidence regarding the genotoxicity of IPA is mixed. While negative results have been consistently reported for IPA in studies that use mammalian cell systems, both positive and negative results have been reported in *S. typhimurium* at very high concentrations (5,000-10,000 µg/plate). No data is currently available for IPA in *in vivo* toxicity tests. As a result, data from TPA, indicates that IPA is not likely to be an *in vivo* genotoxicant. In TPA, results from an *in vivo* genotoxicity study (micronuclei formation in mice with doses of 200-800 mg/kg/day) were negative. In a two year bioassay, rats that were fed TPA (greater than 2%) 1000 mg/kg b.w./day developed bladder calculi, bladder hyperplasia and bladder tumors. Fetotoxicity was observed in an oral reproductive toxicity study for TPA (NOAEL (parental and F1 generation) = 240-307 mg/kg/day) with no effects on reproductive performance (NOAEL >2480 mg/kg/day). However, no signs of fetotoxicity or developmental effects were noted following inhalation exposures to IPA (NOAEL = 10 mg/m^3).

Environment

In its ionised form, IPA is a crystalline powder that has a melting point of 347 ^{0}C, sublimes, a vapor pressure of 3.5 x

10^{-6} Pa at 25 ^{0}C, a measured log K_{ow} of –2.34 and a water solubility of 5400 mg/L at 25 ^{0}C. In IPA's non-ionized form the log Kow is 1.76 and has a water solubility of 130 mg/L at 25 ^{0}C. IPA is not persistent in the environment and is not expected to bioaccumulate in food webs. The half-life of IPA in air is estimated to be 8 to 12 days due to direct reactions with photochemically generated hydroxyl radicals. IPA is readily biodegraded under aerobic and anaerobic conditions. Limited environmental monitoring data suggest that ambient levels of IPA in air are low with levels ranging from 1.3 – 3.4 ng/m^{3} in California and Japan (background levels were estimated to be 0.03 ng/m^{3}). Based on IPA's physical chemical properties, IPA will partition primarily to the water compartment, whether in its ionised or non-ionised form. Acute toxicity testing in fish, invertebrates, and algae indicate low toxicity with no effect concentrations of >895, >876 and >969 mg/l (the highest concentration tested for all test species), respectively.

Exposure

IPA is mainly used in the synthesis of resins, and in packaging fibers and plastics. In 1998, U.S. production was approximately 100,000 metric tonnes. Approximately 70% of the IPA produced is used in coatings and resins, while the remaining 30% is used in packaging fibers and fabrics. Exposures to workers may occur via inhalation and dermal contact. Because IPA present in consumer products is bound in a polymer matrix, the potential for exposures to consumers is low. Additionally, because IPA is not persistent in the environment, the potential for environmental exposures is low.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

No further work is recommended.

SIDS FULL SUMMARY

CAS NO.: 121-91-5		SPECIES	PROTOCOL	RESULTS
PHYSICAL CHEMISTRY				
2.1	Melting Point		Measured	347° C 345-348° C 341-343° C
2.2	Boiling Point			Sublimes
2.3	Density		Measured	1.5 g/ml
2.4	Vapor Pressure		Measured Estimate MPBPWIM version 1.4	9 Pa at 100° C, 3.5 x 10-6 Pa at 25ºC
2.5	Partition Coefficient		OECD 107	Log Kow = -2.34 (at pH =7)
			Estimate	Log Kow = 1.66
			Estimate KOWWIN v1.66	Log Kow = 1.76
2.6	Water Solubility		Measured	130 mg/l at 25° C
	pKa			pKa1 = 3.70 pKa2 = 4.60
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		Estimate AOPWIN	Half-life: 8.2 days
3.2	Monitoring Data		Measured	Detected in air: 2.1-3.4 ng/m^3
3.3	Environmental fate & distribution		Estimate Fugacity Level I Level II Level III	 Air – 0.00009% Water – 99.9% Soil - 0.00041% Air – 0.00009% Water – 99.9% Soil – 0.00041% Air – 0.000013% Water – 76.1% Soil – 23.8%
3.5	Biodegradation		Modified Sturm	>60% within 7 days
3.7	Bioaccumulation		Estimate	BCF = 2
ECOTOXICOLOGICAL DATA				
4.1	Acute Fish	Leuciscus idus melanotus	OECD 203	96-hour NOEC > 895 mg/l
4.2	Acute Daphnid	Daphnia magna	OECD 202	48-hour EC_0 > 876 mg/l
4.3	Acute Aquatic Plant	Scenedesmus subspicatus	OECD 201	96-hour NOEC >969 mg/l
4.4	Toxicity to Bacteria	Activated sludge	OECD 209	EC5 – 158.3 mg/l, EC25 – 353.3 mg/l, EC50 – 617 mg/l, EC75 – 1077 mg/l, EC95 – 2405 mg/l

CAS NO.: 121-91-5		SPECIES	PROTOCOL	RESULTS
MAMMALIAN TOXICOLOGICAL DATA				
5.1.1	Acute Oral	Rat	Acute Oral Toxicity	LD50 > 5,000 mg/kg LD50 13,000 mg/kg LD50 10,900 mg/kg LD50 10,400 mg/kg
5.1.2	Acute Inhalation	Rat	Acute Inhalation Toxicity	LC50 > 11.37 g/m3
5.1.3	Acute Dermal	Rabbit	Acute Dermal Toxicity	LD50 > 2000 mg/kg LD50 > 23,000 mg/kg
5.1.4	Acute Other Routes	Rat Mouse	LD50	i.p. LD50 13,000 mg/kg i.p. LD50 4200 mg/kg
5.2.1	Skin Irritation	Rabbit	Skin Irritation	Negative
5.2.2	Eye Irritation	Rabbit	Eye irritation	Negative
5.2.3	Skin Sensitization	Guinea Pig	Modified Buehler	Not a sensitizer
5.4	Repeated Dose	Rat Rat	13-feeding study 4-Week Inhalation study	13-week feeding study: Slight increase in the incidence of crystalluria (1/25 male, 2/25 female) and renal pathology (mild hydronephrosis, pelvic calcification 5/25 males). NOAEL = 0.5% or 250 mg/kg-day, LO AEL = 1.6% or 800 mg/kg-day. 4-week inhalation study– No significant effects up to 10 mg/m^3 6 hours per day 5 days per week. NOAEL > 10 mg/m^3.
5.5	Genetic Toxicity In Vitro			
A	Bacterial	Salmonella typhimurium Salmonella typhimurium Salmonella typhimurium	OECD 471 OECD 471 OECD 471	No mutagenic activity with or without metabolic activation. Dose dependent increase in the number of revertants with strains TA1537, TA1538, and TA98 in the presence and absence of metabolic activation. Positive response with tester strains TA98 and TA1538 in the presence of activation and with tester strains TA1538 in the absence of microsomal activation.
B	Non-Bacterial	Chinese Hamster Ovary cells Chinese Hamster Ovary cells Mouse lymphoma L5178Y cells	In vitro Chromosomal Aberration (OECD 473). In vitro HGPRT mutation (OECD 476). Mouse Lymphoma mutation (OECD 476)	Negative in the presence and absence of metabolic activation. Negative in the presence and absence of metabolic activation. No evidence of mutagenic activity in the presence and absence of metabolic activation.

5.6	Genetic Toxicity In vivo	Mouse	Chrom Aberration (OECD 474)	Negative for the structurally similar compound terephthalic acid (CAS NO. 100-21-0)
5.7	Carcinogenicity	Rat (Fischer 344)	2-year feeding study	For animals fed the structurally similar compound terephthalic acid (0, 20, 142 or 1000 mg/kg/day) there was a compound related increase in tumors, and hyperplasia of the urinary bladder at the highest dose tested and only in females.
5.8	Reproductive Toxicity	Rat (Wistar and CD)	90-day feeding study/1-gen reproductive assessment	For the structurally similar compound, terephthalic acid, no effects on fertility in a one-generation feeding study up to 5% in the diet (2499-2783 mgkg/d). Fetotoxic effects at 2% (930-1107 mg/kg/d) and 5% that included postnatal deaths, decreased survivability, high incidence of renal and bladder calculi and histopathological sequelae associated with presence of the calculi. NOEL for maternal and fetotoxic effects 0.5% (240-282 mg/kg/d).
5.9	Developmental Toxicity/Teratogenicity	Rat	Segment II Inhalation Teratology Study	No maternal or developmental toxicity at inhalation exposures up to 10 mg/m^3, days 6-15 of pregnancy.
5.10	Toxicokinetics	Rat Rat		Blood levels of IPA collected during a 13-week feeding study increased in a dose dependent manner. 24-hour urinary excretion data collected on days 7, 30, 60, 90 indicate that urinary excretion, presumably as the unchanged chemical, is the primary mechanism by which IPA is excreted. Blood levels of IPA were detected immediately following exposure to 10 mg/m^3, 6 hours per day. Serum levels were 5.3-9.3 ug/ml in females and 1.4-3.4 ug/ml for males. Data suggest that a steady state is achieved on first day of exposure. One week following exposure, IPA was not detected in the blood.

SIDS Initial Assessment Report (SIAR)

1.0 IDENTITY

Isophthalic acid (121-91-5) or IPA is a crystalline powder that possesses the following physical-chemical properties and characteristics:

Property	Value
Chemical Formula	$C_8H_6O_4$
Molecular Weight	166.13
Purity	99.9%
Impurities	Reaction intermediates (3-formylbenzoic acid and m-toluic acid); by-products (benzoic acid); and residual metals
Melting Point	347 °C
Boiling Point	Sublimes
Density	1.5 g/mL at 20 °C
Vapor Pressure Partition Coefficient (Log K_{ow})	3.5×10^{-6} Pa at 25 °C (calculated) -2.34* at pH 7 1.76 (neutral form)
Water Solubility	5400 mg/L at 25 °C 130 mg/L at 25 °C **
Synonyms	Benzene-1,3-dicarboxylic acid m-phthalic acid isophthalate m-benzenedicarboxylic acid

* Log Kow –2.34 is believed to be the most relevant value as IPA will be ionized under most environmental conditions.

** This value represents the solubility of of IPA without adjustment of pH. The pH of the water was not specifically stated though the pH of distilled water is typically between 6.0 and 7.0 depending on the amount of dissolved gas.

IPA is a dibasic acid (with two displaceable hydrogen atoms), and consequently has two dissociation constants (pKa1 = 3.70; pKa2 = 4.60 at 25 °C).

IPA is closely related in structure to terephthalic acid (TPA; CASRN=100-21-0). IPA and TPA are isomers, differing only with respect to the positioning of their carboxylic acid groups on the benzene ring (1,3- and 1,4-, respectively). The physical-chemical properties, metabolism pathways, and toxicological properties of IPA and TPA are very similar.

2.0 GENERAL INFORMATION ON EXPOSURE

The manufacture of IPA is accomplished using a continuous, enclosed process. Solvents, catalysts, and water used in the manufacture of IPA are recycled. Meta-xylene is used to synthesize crude IPA, in the form of an off-white powder. IPA is then purified to form a white powder, which is stored in silos and transferred using bulk trucks, railcars, or packaged in 1 metric tonne or 50 lb bags for sale. Waste streams are routed to an on-site wastewater treatment plant. Because manufacture occurs within a closed system, little to no IPA is expected to be released to the environment during production.

Estimated National Production or Import Volume

In 1998, U.S. production of IPA was approximately 100,000 tonnes (Personal Communication with BP Amoco, 2001). In the early- to mid-1970s, U.S. production of IPA typically ranged from 42 to 54 thousand tonnes (SRI, 1972, 1975). Production capacity in the U.S. in the 1980s was 250,000 tons/year (230,000 tonnes/year) (Gerhartz, 1985).

Although U.S. imports of IPA were negligible in the 1970s (SRI, 1972), significant amounts (41,000 tonnes/year) were imported during the 1980s (Bureau of the Census, 1984).

U.S. exports in the 1970s typically ranged from 1.3 to 4.4 thousand tonnes/year (SRI, 1972, 1975).

Uses and Functions

Of the IPA produced in the U.S. in 1998, approximately 70% was used in coatings and resins, while the remaining 30% was used in packaging fibers and fabrics (Personal Communication with BP Amoco, 2001). Approximately 54% of the IPA produced in the 1970s was reported to be used in the synthesis of isophthalic polyester resins, approximately 26% was used for alkyd resins production, approximately 1% as a chemical intermediate for the production of dioctyl isophthalate, and the remaining (approximately) 19% was used for other applications (SRI, 1972, 1975).

Form of Marketed Product

IPA forms part of a polymer matrix in a wide variety of products in the form of coatings, resins, packaging fibers, and fabrics.

Sources of Potential Release to the Environment

IPA is naturally occurring, with traces detected in lignite and in the rhizome of the iris plant (Bemis *et al.*, 1982). Additionally, IPA was found to be an oxidation product of Singletary Lake fulvic acid (Christman *et al.*, 1985). Data on natural sources are extremely limited, and a meaningful comparison with anthropogenic releases is not possible.

Isophthalic acid may be released to the environment in wastewater as a result of its production and use as a chemical intermediate for unsaturated polyester resins (Kramer, 1992), thermoplastic polyesters (Bruegging and Rueter, 1992), and alkyd resins (Lin, 1992).

Dicarboxylic acids produced by photooxidation of anthropogenic compounds during long-range transport are a source of IPA in atmospheric aerosols (Satsumabayashi *et al.*, 1990). There are also industrially important esters of IPA such as dimethyl isophthalate that may undergo chemical or enzymatic hydrolysis to yield IPA (Riemenschneider, 1987; NRCC, 1980; Wolfe *et al.*, 1980).

2.1 Environmental Exposure and Fate

Using default release estimates, predictions based on fugacity-based fate and transport models (Levels 1 and 2: Trent University, 1999) suggest that the majority of the IPA released to the environmental will partition primarily to the water compartment (99.9%), with negligible amounts found in the air, soil, and sediment compartments. Based on a Level 3 fugacity model (Trent University, 1999), the majority (76.1%) of IPA released is again predicted to partition to the water compartment. However, a larger percentage (23.8%) is predicted for soil, since this model level allows for continuous release to soil, with negligible amounts partitioning to air (<1%) and sediment (<1%).

Biodegradation IPA is readily biodegradable in screening tests using sewage sludge and may be expected to biodegrade in soil. Under aerobic conditions and following OECD guideline 301B, approximately 9%, 46%, 64%, and 77% of IPA contained in sludge was degraded after 2, 5, 7, and 12 days, respectively (Battelle, 1991). Similarly, IPA is degraded by aerobic microorganisms isolated from soil and marine sediment (Keyser *et al.*, 1976; Aftring *et al.*, 1981). Cultures isolated from marine sediments also degraded IPA under anaerobic conditions, although by a different metabolic pathway. After a 24-hour acclimation to an activated sludge inoculum, 84% of IPA was consumed in a respiratory test (Lund and Rodriguez, 1984). In another screening test, 95% of chemical oxygen demand (COD) was removed over five days using an acclimated activated sludge inoculum (Pitter, 1976). In a 2-week biodegradation-screening test using 100 ppm IPA and an activated sludge inoculum, 77.1% of BOD was removed (Japan Chemical Industry Report, 1992). Another investigator confirmed that IPA was significantly biodegradable using the screening test (Kitano, 1978). IPA was completely degraded in eight days using a soil inoculum (Alexander and Lustigman, 1966).

Terrestrial Fate

Based on its chemical-physical properties, IPA is expected to be highly mobile in soil (Meylan *et al.*, 1992; Swann *et al.*, 1983). In the environment, IPA is expected to be dissociated to form salts with cations in soil. Because IPA absorbs UV radiation >290 nm (Sadtler Research Laboratories, as cited in HSDB, 2001), it may photodegrade in surface soils.

Aquatic Fate

Based on its chemical structure, IPA is not expected to undergo abiotic hydrolysis in the environment. Under environmentally relevant conditions (pH) IPA is expected to partially dissociate resulting in the formation of isophthalic acid salts. In addition, based on its chemical-physical properties, IPA is not expected to adsorb to sediment and particulate matter in the water column. The very low Henry's Law constant estimated for IPA (4.4E-11 atm-m^3/mole [HENRYWIN USEPA EPI v3.10]) suggests that volatilization from surface water will be minimal. Since IPA is biodegradable in screening tests (Japan Chemical Industry Report, 1992; Pitter, 1976), it may also biodegrade in water. The absorption of UV radiation >290 nm (Sadtler Research Lab, 1990) suggests that IPA may also directly photodegrade in surface waters. A bioconcentration factor (BCF) value of 2 estimated for IPA (Lyman et al. 1982), suggests that IPA would not be expected to bioconcentrate in aquatic organisms.

Atmospheric Fate

IPA in the atmosphere exists in both the vapor and particulate phases (Cautreels and Cauwenberghe, 1978; Yokouchi and Ambe, 1986). IPA in the vapor-phase is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 12.3 days (Meylan and Howard, 1993). Similarly, a half-life of 8.2 days has been estimated for IPA based on

reaction with hydroxyl radicals using the AOPWIN software to assess its atmospheric oxidation potential (SRC, 2001). IPA in the particulate-phase may be physically removed from the air by wet and dry deposition processes.

2.2.1 Human Exposure

Information regarding potential occupational, consumer, and indirect exposures to IPA is provided below.

Occupational Exposure

Based on the manufacturing process, significant occupational exposure during normal operating procedures is not anticipated. Some potential for occupational exposure via the inhalation and dermal routes is possible during bag filling operations and while loading rail cars and trucks. Typical exposures for unit operators, baggers/loaders and forklift operators working in IPA manufacturing range from <0.04 to 2.92 mg/m^3 (personal communication BP Amoco) Engineering controls are employed to reduce employee exposure. In addition, appropriate personal protective equipment is generally available and may be worn to further reduce potential exposure. Information regarding downstream occupational exposures in not publicly available.

Occupational exposure limits (OELs) for IPA are listed below.

Exposure Limit (Country)	(mg/m^3)	(ppm)
Workplace environmental exposure level, 8-hr time-weighted average (U.S.)	10 (total) 5 (respirable)	1.5 0.74
STEL (Russia)	0.2 mg/m3	0.03

Consumer Exposure

Because IPA forms part of a polymer matrix in marketed products, the potential for consumer exposure to IPA is low. Some of these polymer matrices containing reacted isophthalic acid as a component have food contact applications. However, this accounts for less than 20 percent of the IPA use. Furthermore, result from measurements of residual IPA levels and migration into food simulant studies indicated that IPA residual levels were in the part per billion range and extraction into to food simulants were below detection limits (personal communication BP Amoco).

Indirect Exposure via the Environment

The ambient annual average concentrations of IPA in fine particle organic compounds at four sites in California on a west to east trajectory, West Los Angeles, downtown Los Angeles, Pasadena, and Rubidouc for 1982 were 2.1, 3.4, 2.9 and 2.1 ng/m^3, respectively (Rogge et al. 1993). The concentration of IPA at a background site on San Nicolas Island, west of Los Angeles, averaged <0.03 ng/m^3 from July to December (Rogge *et al.*, 1993).

A study was performed of the long-term transport of air pollution from large emission sources along the coastal areas in Japan to inland mountains (Satsumabayashi et al. 1990). The resulting mean concentrations of IPA in airborne aerosols in a plume at Takasaki (July 26-31, 1986) and Karuizawa (July 29-31, 1986) were 2.2 and 1.3 ng/m^3, respectively. The ratio of carboxylic acids to acetylene (which is believed to be derived from the same sources) increased during the day and decreased at night and averaged 72% at

Takasaki and 84% at Karuizawa. The authors proposed that IPA is almost entirely formed photochemically during long-term transport of airborne aerosols.

3.0 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

Information regarding the toxicity of IPA are summarized below. Where information on IPA is lacking, supplemental information for a structural isomer, terephthalic acid or TPA, (CAS:100-21-0) is provided. TPA is an isomer of IPA, differing only with respect to the positioning of the carboxylic acid groups on the benzene ring (1,3- for IPA; 1,4- for TPA). Both IPA and TPA are readily eliminated from the body, largely unchanged, via urinary excretion. The toxicities of these two isomers are also very similar with the formation of urinary calculi and subsequent inflammatory changes of the urinary tract being the only notable effect after repeated oral ingestion.

Toxicokinetics and Metabolism

Blood levels of IPA and TPA (determined as total mg phthalate/L) collected during a 13-week feeding study (in rats) were increased in a dose-dependent manner on days 7, 30, 60, and 90. IPA and TPA blood levels were generally highest during the first week of exposure and declined during the course of the study, suggesting either a change in feed consumption rates or some sort of adaptation resulting in increased clearance from the body. Results from 24-hour urines collected on days 7, 30, 60, and 90 indicate that urinary excretion, presumably as unchanged chemical, is the primary route of elimination for both IPA and TPA (Vogin, 1972).

Blood levels of IPA were detected immediately following exposure to rats at 10 mg/m^3 for six hours/day (IITRI, 1988). These levels remained elevated throughout the exposure period. Serum IPA concentrations detected in female rats (5.3-9.3 µg/mL) were consistently higher than the concentrations detected in male rats (1.4-3.4 µg/mL). The data suggest that steady state is achieved fairly rapidly (on the first day of exposure). One week following exposure, IPA was not detected in blood, indicating that clearance of IPA from the body occurs fairly rapidly. Based on a log K_{ow} value of –2.34, IPA is not expected to accumulate appreciably in tissues, and is likely to be readily excreted from the body.

In a similar study, rats were exposed via inhalation to an aerosol of 10 mg/m^3 TPA six hours per day for 25 consecutive days followed by a 28-day recovery period. Detectable blood concentrations of TPA were observed after 10 days of exposure and progressively increased over the remaining exposure period. The highest average blood concentration was 2.7 µg/mL after 25 days. Seven days after completion of the exposure period the blood concentration was less than 1 µg/mL (IITRI 1989).

Based on a molecular weight of 166 g/mol and a log Kow of –2.34, a dermal permeability coefficient (K_p) of 4.0x10^{-6} cm/hr was estimated for IPA (USEPA, 1992). This value suggests that the dermal absorption of IPA from an aqueous solution is relatively low.

IPA was reported to be a competitive inhibitor of hepatic glutamate dehydrogenase in cows (Boots *et al.*, 1976). This enzyme plays an important role in amino acid catabolism, amino acid synthesis, and nitrogen balance.

Acute Toxicity

Data available from laboratory animals exposed to IPA indicate that its acute toxicity is relatively low, regardless of the route of exposure.

- *Oral* – Acute oral LD50 ranging from values of 10,400 to 13,000 mg/kg for IPA have been reported in rats (Marhold, 1986; Industrial Bio-Test, 1958, 1975). Necropsy of animals that died revealed pale, discolored kidneys (Industrial Bio-Test, 1975). No deaths were reported in rats receiving a single oral dose of 5,000 mg/kg IPA (IITRI, 1990). Clinical signs (irritability, salivation, discoloration around nose and mouth, diarrhea, wet and/or discolored inguinal fur, discolored paws), which appeared within 24 hours after exposure, but generally resolved within 48 hours.
- *Inhalation* – No deaths or treatment-related effects were observed in rats exposed to 11,400 mg/m^3 IPA dust for four hours (Industrial Bio-Test, 1958).
- *Dermal* – In rabbits, no deaths were reported following a single dermal dose of 2000 mg/kg or 23,000 mg/kg IPA (IITRI, 1990; Industrial Bio-Test, 1958).
- *Other* – Following intraperitoneal injection, LD50 values of 4,200 and 13,000 mg/kg have been reported for IPA in mice and rats, respectively (Academie des Sciences, 1965; Calandra, 1975)

Irritation/Corrosiveness

IPA has negligible skin irritation potential and is only slightly irritating to eyes. No signs of dermal irritation (irritation score=0/8) was evident in rabbits receiving a single dermal dose of 500 mg IPA (IITRI, 1990). Mild dermal irritation (erythema) was observed in 4/10 immediately following dermal exposure to 2,000 mg/kg IPA (IITRI, 1990). Eye irritation scores ranging from 5.3/110 to 25.6/110 at 24 hours have been reported. In all cases signs of irritation were completely resolved by the end of the study.

Skin Sensitization

In guinea pigs dermally exposed to 0.3 mL of a 30% IPA solution once a week for three weeks, a positive erythema reaction (a score greater than or equal to 2) was observed in only 1/10 animals, and was not considered significant (IITRI, 1991). The authors concluded that repeated exposure to IPA did not produce dermal sensitization. Furthermore, no reports of human skin sensitization were located. The data suggest that IPA is unlikely to cause allergic skin reactions.

Repeated Dose Toxicity

Data available from laboratory animals exposed to IPA indicate that its subchronic toxicity is also relatively low, regardless of the route of exposure.

- *Oral* – In Wistar rats exposed to up to 0.5% IPA in feed (corresponding to a dose of approximately 250 mg/kg-day) for 13 weeks, no adverse effects were observed (Vogin, 1972). Levels of 1.6% (approximately 800 mg/kg-day) in feed produced small increases in the incidence of crystalluria (1/25 males, 2/25 females) and renal pathology (mild hydronephrosis, pelvic calcification, 5/25 males). This study identifies a NOAEL and LOAEL of 250 and 800 mg/kg-day, respectively, based on kidney effects in rats.
- *Inhalation* – Sprague-Dawley Rats were exposed to 1.0, 5.0 or 10 mg/m^3 IPA particulate aerosol for six hours/day, five days/week for four weeks. No treatment-related effects were reported for body weight gain, organ weights, hematology, or clinical chemistry parameters (IITRI, 1988). This study identifies a NOAEL of 10 mg/m^3 for subchronic inhalation exposures to IPA.

Genetic Toxicity

Although no studies regarding the *in vivo* genotoxicity of IPA were located, information collected for a structural isomer, TPA, is available. The number of micronuclei induced in the erythrocytes of mice exposed to a single i.p. dose of 200-800 mg/kg-day TPA was not increased (Bioreliance, 2001).

In mammalian cell systems, test results for the genetic toxicity of IPA are consistently negative. In Chinese hamster ovary cells, IPA concentrations up to 5000 ug/L, with and without metabolic activation, did not produce an increase in chromosomal aberrations (Microbiological Associates, 1990). Similar results were noted in this cell system when IPA concentrations up to 3,000 µg/L were evaluated for mutations at the HGPRT locus (Microbiological Associates, 1991). No increase in mutation frequency was reported in mouse lymphoma cells using test concentrations up to 950 µg/L (Riach and Willington, 1994).

Evidence regarding the genetic toxicity of IPA in bacteria cell systems is mixed. Three separate gene mutation studies with Salmonella typimurium were performed.. Each study was conducted both in the absence and presence of an exogenous metabolic activation system. The maximum dose of IPA investigated in two of the studies was 10,000 ug/plate, while the third study evaluated dose levels up to 5000 ug/plate. IPA-220 concentrations of up to 5000 µg/plate, with or without metabolic activation (rat liver S9), did not result in an increased mutation frequency in several strains of *Salmonella typhimurium* (TA1535, TA1537, TA1538, TA98, and TA100) (Huntingdon Research Centre, 1991). However, a small increase in mutation frequency was observed in two strains of *S. typhimurium*: TA98 (3-fold increase with activation) and TA1538 (9-fold increase with activation, and 6-fold increase without activation) using concentrations up to 10,000 µg/plate (Microbiological Associates, 1990). Precipitation of IPA was noted at concentrations higher than 5,000 µg/plate. No increase in mutation frequency was noted in these two strains at IPA concentrations less than or equal to 1,000 µg/plate, or in strains TA100 or TA1535 at IPA concentrations up to 10,000 ug/plate. In another experiment, concentrations up to 10,000 µg/plate resulted in an increased mutation frequency in several strains of *S. typhimurium*, including TA98 (7-fold increase with activation, 4-fold without activation), TA1537 (7-fold with and without activation), and TA1538 (10-fold with activation, 11-fold without activation) (Muller, 1991). No increase in mutation was observed in these test strains at IPA concentrations less than or equal to 500 µg/plate, or in strains TA100 or 1535 at IPA concentrations up to 10,000 µg/plate. It is noteworthy that both studies yielding positive responses evaluated dose-levels up to 10,000 ug/plate. At dose-levels of 5,000 ug/ml and above there is a clear indication in the report from one study that IPA visibly precipitated in the plates and the bacteria lawn was adversely affected.

The assays for gene mutation in bacteria produced inconsistent and equivocal results, though all three studies were considered valid. Thus the mutagenic potential of IPA in bacterial systems could not be determined definitively. In contrast, IPA elicited negative responses in assays investigating gene mutation in two different mammalian cell systems and chromosomal aberration in mammalian cells. In addition, IPA has no apparent structurally alerts. Furthermore, TPA (the structural analog of IPA) did not induce an increase in the mutation frequency of *Salmonella typhimurium*. Bacteria are relatively simple organisms, and a positive response in bacteria does not necessarily indicate that the compound will induce similar effects in animal cells or in intact mammals. Moreover when evaluating genetic toxicity assay results *in vivo* test results are considered to have greater weight than *in vitro* tests, tests in eukaryotes are considered to have greater weight than prokaryotes and tests using mammalian species are considered to have greater weight than tests using non-mammalian species. Therefore, the weight of evidence suggests that IPA is not mutagenic in mammalian cells and is unlikely to be active in a whole animal.

Carcinogenicity

No data regarding the carcinogenicity of IPA were located. However, a chronic dietary studies on the structural analog TPA are available. A two-year feeding study (0, 20, 142, or 1000 mg/kg/day) showed increase incidence of calculi, bladder hyperplasia and tumors in rats. These effects were seen only at the highest dose of 1000 mg/kg/day and only in females (CIIT 1983). In a similar study by Gross 1974 bladder and ureter tumors were reported for both males and females. The difference in male tumor response may be partially explained by the higher doses used in the Gross study (500, 1000, 2500 mg/kg/day). The induction of bladder tumors is believed to be a result of injury to the bladder epithelium from calculi formation.. Bladder calculi cannot occur unless the solubility of the stone components is exceeded. Based on urinary solubility of Ca-terephthalate, normal urine would become saturated with Ca-terephthalate at a terephthalic acid concentration of approximately 8 to 16 mM. Assuming that the average volume of urine excreted by humans is 1.5 liters/day, the amount of terepthalic acid that would have to be absorbed to produce the minimum saturating concentration of terephthalica acid is 2400 mg/day. It is unlikely that humans would ingest enough TPA to induce bladder calculi and therefore of low concern to human health. Based on similar findings from repeat dose studies with IPA and TPA (crystalluria) it is expected that IPA would respond similar to that of TPA with respect to carcinogenicity.

Reproductive Toxicity

Although no studies regarding the reproductive toxicity of IPA were located, information collected for a structural isomer, terephthalic acid (TPA), is available. In a one-generation reproductive toxicity test using two strains of rats (CD and Wistar), exposure to TPA in the diet at levels of 0, 0.03, 0.125, 0.5, 2 or 5% (approximately equivalent to: 0, 14, 59, 240, 930, 2499 mg/kg-day CD males; 0, 17, 67, 282, 1107, 2783 mg/kg/day CD females; 0, 14, 61, 249, 960, 2480 mg/kg/day Wistar males and; 0, 19, 78, 307, 1219, 3018 mg/kg/day Wistar females) began 90 days prior to mating, and continued through gestation and lactation (Gibson, 1982). Food intake and body weight gain were decreased in animals at the two highest dietary levels. Five deaths were reported in rats receiving the highest dietary level. Reproductive performance in parental animals was not affected by exposure (NOAEL 5.0% or 2480-3018 mg/kg/day). However, in the offspring, significant decreases in survival and body weight, and a significant increase in the incidence of renal/bladder calculi were observed at levels of 2% and 5%. Several large litters of pups were lost to dams suffering obvious signs of toxicity. Several of these dams did not allow the pups to nurse and did not attend the litters. This study identifies NOAEL and LOAEL values of 240-307 mg/kg/day (0.5%) and 930-1219 mg/kg-day (2.0%), respectively, for both maternal and fetotoxicity in rats.

Developmental Toxicity/Teratogenicity

No evidence of teratogenesis or fetotoxicity was observed in rats exposed to 0, 1, 5, or 10 mg/m^3 IPA particulate aerosol on gestation days 6 through 15 (IITRI, 1991). As summarized for the reproductive toxicity study above, oral doses of 930-1219 mg/kg-day of TPA administered in the diet for 90 days were fetotoxic (Gibson, 1982). The most likely route of potential exposure to IPA is via inhalation during manufacture and use. Therefore, the IPA inhalation study is likely more relevant than the oral TPA study for assessing fetotoxicity.

Human Cases

No data were located regarding human exposures or responses to IPA.

4.0 HAZARDS TO THE ENVIRONMENT

4.1 Acute Aquatic Effects

Data regarding the acute toxicity of IPA in aquatic species are summarized below.

- *Fish* - No signs of toxicity were observed in *Leuciscus idus melanotus* (Golden orfe) exposed to IPA at levels of up to 895 mg/L (measured) for 96 hours under static conditions (Battelle Europe, 1993).
- *Invertebrates* - No signs of toxicity in terms of mortality or immobilization were observed in *Daphnia magna* (water flea) exposed to IPA at levels of up to 876 mg/L (measured) for 48 hours under static conditions (Battelle Europe, 1993).
- *Plants* - No adverse effects on growth were observed in *Scenedesmus subspicatus* (green algae) exposed to IPA at levels of up to 969 mg/L (measured) for 96 hours under static conditions (Battelle Europe, 1993).
- *Bacteria* - In activated sewage sludge, toxicity to bacteria, as indicated by inhibition of oxygen consumption, was evident with a EC50 value of 617 mg/l (Battelle Europe, 1991).

Because IPA is an acid, adjustments were made to the testing systems in the studies above, to ensure that neutral pH is maintained. For this reason, the predominant form of the chemical tested was likely to be isophthalic sodium salt. In general, these data indicate low acute toxicity of IPA in aquatic species.

4.2 Terrestrial Effects

Although no data were located regarding the toxicity of IPA in terrestrial mammals, the low toxicity in laboratory animals suggests that its toxicity to mammals in general would also be low.

4.3 Other Environmental Effects

A bioconcentration factor (BCF) of 2 has been estimated for IPA, which suggests that IPA is not likely to concentrate in tissues or bioaccumulate in food webs.

5.0 CONCLUSIONS AND RECOMMENDATIONS

IPA is currently of low priority for further work.

Analog Jusitification

For most SIDS endpoints, adequate data are available for IPA to provide a characterization of its toxicity. Due to not having sufficient data for the endpoints of reproductive toxicity and in vivo genotoxicity with IPA, information on terephthalic acid (or TPA, CAS:100-21-0), an isomer of IPA was used as a surrogate. IPA and TPA are structural isomers, with carboxylic acid groups on the benzene ring at 1, 3- and 1,4-carbons, respectively. Both IPA and TPA have similar physicochemical properties and show similar metabolic pathways and toxicological properties.

Human Health

In rats, both IPA and TPA are eliminated from the body unchanged primarily via urinary excretion. A steady state in blood is achieved fairly rapidly after inhalation exposure (on the first day) to IPA. One week after cessation of exposure, IPA was no longer detectable in the blood. Based on the Log Kow (-2.34), IPA is not expected to accumulate appreciably in tissues and is likely to be readily excreted from the body.

IPA exhibits low acute toxicity by the oral, dermal, and inhalation routes. The oral LD50 has been reported from >5000 mg/kg (no deaths) to 13,000 mg/kg in rats. No mortality was observed in rats following acute inhalation exposures to 11,400 mg/m^3 or acute dermal doses in rabbits of 23,000 mg/kg. IPA is not a skin sensitizer as skin reactions were only seen in 10% of the animals. IPA has negligible skin irritation potential and was considered slightly irritating to the eyes.

In repeated dose studies, the target organ is the kidney. For IPA, a NOAEL of 250 mg/kg-day for kidney effects (crystalluria, mild hydronephrosis, pelvic calcification) has been reported for rats following repeated oral exposures. No systemic effects were observed in rats following repeated inhalation exposures to 10 mg/m^3 of IPA. Evidence regarding the genotoxicity of IPA is mixed. While negative results have been consistently reported for IPA in studies that use mammalian cell systems, both positive and negative results have been reported in *S. typhimurium* at very high concentrations (5,000-10,000 µg/plate). No data is currently available for IPA in *in vivo* toxicity tests. As a result, data from TPA, indicates that IPA is not likely to be an *in vivo* genotoxicant. In TPA, results from an *in vivo* genotoxicity study (micronuclei formation in mice with doses of200-800 mg/kg-day) were negative. In a two year bioassay, rats that were fed TPA (greater than 2%) 1000 mg/kg b.w./day developed bladder calculi, bladder hyperplasia and bladder tumors. Fetotoxicity was observed in an oral reproductive toxicity study for TPA (NOAEL (parental and F1 generation) = 240-307 mg/kg-day) with no effects on reproductive performance (NOAEL >2480 mg/kg-day). However, no signs of fetotoxicity or developmental effects were noted following inhalation exposures to IPA (NOAEL = 10 mg/m^3).

Environment

In its ionised form, IPA is a crystalline powder that has a melting point of 347^{0}C, sublimes, a vapor pressure of 3.5 x 10^{-6} Pa at 25^{0}C, a measured log K_{ow} of –2.34 and a water solubility of 5400 mg/L at 25^{0}C. In IPA's non-ionized form the log Kow is 1.76 and has a water solubility of 130 mg/L at 25^{0}C IPA is not persistent in the environment and is not expected to bioaccumulate in food webs. The half-life of IPA in air is estimated to be 8 to 12 days due to direct reactions with photochemically generated hydroxyl radicals. IPA is readily biodegraded under aerobic and anaerobic conditions. Limited environmental monitoring data suggest that ambient levels of IPA in air are low with levels ranging from 1.3 – 3.4 ng/m^3 in

California and Japan (background levels were estimated to be (0.03 ng/m^3.) Based on IPA's physical chemical properties, IPA will partition primarily to the water compartment, whether in its ionised or non-ionised form. Acute toxicity testing in fish, invertebrates, and algae indicate low toxicity with no effect concentrations of
>895, >876 and >969 mg/l (the highest concentration tested for all test species), respectively.

Exposure
IPA is mainly used in the synthesis of resins, and in packaging fibers and plastics. In 1998, U.S. production was approximately 100,000 metric tonnes. Approximately 70% of the IPA produced is used in coatings and resins, while the remaining 30% is used in packaging fibers and fabrics. Exposures to workers may occur via inhalation and dermal contact. Because IPA present in consumer products is bound in a polymer matrix, the potential for exposures to consumers is low. Additionally, because IPA is not persistent in the environment, the potential for environmental exposures is low.

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SIDS DOSSIER
ISOPHTHALIC ACID

.....

CAS No. 121-91-5

Sponsor Country: U.S.A.

DATE: January, 2002

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Note: ; Data elements in the SIDS
; Data elements specially required for inorganic chemicals

1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

A. **CAS-Number** 121-91-5

B. **Name** *(IUPAC name)* Isophthalic Acid

C. **Name** *(OECD name)*

D. **CAS Descriptor**

E. **EINECS-Number** 204-506-4

F. **Molecular Formula** C8-H6-O4

G. **Structural Formula** C8H6O4

H. **Substance Group**

I. **Substance Remark**

J. **Molecular Weight** 166.13

1.02 OECD INFORMATION

A. **Sponsor Country:** U.S.A.

B. **Lead Organisation:**

Name of Lead Organisation: BP Chemicals
Contact person: David Dutton
Address:

U.S.A.
Tel:
Fax:

1.1 GENERAL SUBSTANCE INFORMATION

A. **Type of Substance** element [ ]; inorganic [ ]; natural substance [ ]; organic [X]; organometalic [ ]; petroleum product [ ]

B. **Physical State** *(at 20°C and 1.013 hPa)*
gaseous [ ]; liquid [ ]; solid [X]

C. **Purity** *(indicate the percentage by weight/weight)* 99.9%

1.2 SYNONYMS benzene 1,3-dicarboxylic acid;
m-phthalic acid
isophthalate
m-benzenedicarboxylic acid

1.3 IMPURITIES Reaction intermediates: 3-formalbenzoic acid, m-toluic acid; by-products: benzoic acid; and residual metals

1.4 ADDITIVES None

1.5 QUANTITY In 1998 U.S. production of IPA was approximately 100,000 tonnes. (Personal communication BP Amoco 2001)

1.6 LABELLING AND CLASSIFICATION

Labelling
Type:
Specific limits:
Symbols:
Nota:
R-phrases: None
S-phrases: None
Text of S-phrases:
Remarks:

Classification
Type:
Category of danger:
R-phrases:
Remarks:

1.7 USE PATTERN

A. General

Type of Use: Approximately 70% of Isophthalic acid is used in coatings and resins while the remaining 30% is used in packaging fibers and fabrics

Category: Non dispersive use: Chemical industry use as an intermediate.

Remarks:
Reference: BP Amoco Personal communication 2001

B. Uses in Consumer Products

	Function	Amount Present	Physical State

Remarks: IPA forms part of a polymer matrix in a wide variety of products in the form of coatings, resins, packaging fibers, and fabrics.

Reference:

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type:	WEEL, 8-hr time-weighted average (U.S.)
Value:	10 mg/m3 (total); 5 mg/m3 (respirable)

Type:	STEL (Russia)
Value:	0.2 mg/m3 (skin)

Short term exposure limit value

Value:
Length of exposure period:
Frequency:
Remarks:
Reference:

1.9 SOURCES OF EXPOSURE

(a)
Media of release:
Source:
Remarks:
Reference:

1.10 ADDITIONAL REMARKS

A. Options for disposal

Remarks:
Reference:

B. Other remarks

2. PHYSICAL-CHEMICAL DATA

2.1 MELTING POINT

(a)

Value:	347°C
Decomposition:	Yes [ ] No [ ] Ambiguous [ ]
Sublimation:	Yes [ ] No [ ] Ambiguous [ ]
Method:	
GLP:	Yes [ ] No [ ] ? [X]
Remarks:	
Reference:	Lide, D.R. (ed.) CRC Handbook of Chemistry and Physics. 75th edition. Boca Raton, FL: CRC Press, Inc., 1994-1995. HSDB, 2001

(b)

Value:	345-348°C
Decomposition:	Yes [ ] No [ ] Ambiguous [ ]
Sublimation:	Yes [ ] No [ ] Ambiguous [ ]
Method:	Other
GLP:	Yes [ ] No [ ] ? [X]
Remarks:	
Reference:	Merck, 9th Edition.

(c)

Value:	341-343°C
Decomposition:	Yes [ ] No [ ] Ambiguous [ ]
Sublimation:	Yes [ ] No [ ] Ambiguous [ ]
Method:	
GLP:	Yes [ ] No [ ] ? [X]
Remarks:	
Reference:	Aldrich, 1992-93.

2.2 BOILING POINT

(a)

Value:	100°C
Pressure:	0.068 mm Hg (9 Pa)
Decomposition:	Yes [ ] No [ ] Ambiguous [ ]
Method:	
GLP:	Yes [ ] No [ ] ? [X]
Remarks:	IPA sublimes which brings into question the reliability of this reference.
Reference:	SRC PhysProp Database, 2000

(b)

Value:	Not applicable, IPA sublimes
Pressure:	
Decomposition	Yes[] No [] Ambiguous []
Method:	
GLP:	Yes [] No [x] ? []
Remarks:	

Reference: Lide, D.R. (ed.) CRC Handbook of Chemistry and Physics. 75th edition. Boca Raton, FL: CRC Press, Inc., 1994-1995. HSDB, 2001

2.3 DENSITY

(a)

Type:	Bulk density [ ]; Density [x]; Relative Density [ ]
Value:	1.5 g/mL
Temperature:	20 °C
Method:	
GLP:	Yes [ ] No [ ] ? [X]
Remarks:	
Reference:	Kirk-Othmer (1978-1984), Reported in HSDB 2001.

2.4 VAPOUR PRESSURE

(a)

Value:	9 Pa (0.068 mm Hg)
Temperature:	100°C
Method:	calculated [ ]; measured [ ] Year:
GLP:	Yes [ ] No [ ] ? []
Remarks:	
Reference:	Daubert and Danner (1989), as cited in HSDB (2001)

(b)

Value:	3.5 x10^{-6} Pa
Temperature:	25° C
Method:	Calculated[x]; measured[] Year:
GLP:	Yes []; No[x]
Remarks:	
Reference:	MPBPWIN version 1.40 (USEPA EPIWIN Suite Software)

2.5 PARTITION COEFFICIENT $\log_{10}P_{ow}$

(a)

Log Pow:	-2.34
Temperature:	22 °C
Method:	calculated [ ]; measured [X]
GLP:	Yes [X] No [ ] ? [ ]
Remarks:	Value was measured in pH = 7 buffer, which is believed to be environmentally more relevant.
Test Substance	isophthalic acid
Reference:	IIT Research Institute, 1992.

(b)

Log Pow:	1.66
Temperature:	
Method:	calculated [X]; measured [ ]
GLP:	Yes [ ] No [ ] ? [X]
Remarks:	This value is likely an estimate for the neutral form.
Test Substance	isophthalic acid
Reference:	Hansch and Leo, 1981

(c)

Log Pow	1.76
Temperature:	
Method:	Calculated [X] measured []
GLP:	yes [] No [X]
Remarks:	This calculated value represents the Kow for the neutral form.
Test Substance	..... Isophthalic acid
Reference:	KOWWIN v1.66 (EPIWIN Suite)

2.6 WATER SOLUBILITY

A. Solubility

(a)

Value:	$0.54x10^4$ mg/L
Temperature:	14^oC
Description:	Miscible[ ]; Of very high solubility [ ]; Of high solubility [ ]; Soluble [ ]; Slightly soluble [ ]; Of low solubility [ ]; Of very low solubility [ ]; Not soluble [ ]
Method:	Other
GLP:	Yes [ ] No [ ] ? [X]
Remarks:	This value most likely represents the solubility after adjustment of the pH, forming the more water soluble isophthalic acid salt.
Reference:	Towle et al., 1968.

(b)

Value:	130 mg/L
Temperature:	25^oC
Description:	Miscible[ ]; Of very high solubility [ ]; Of high solubility [ ]; Soluble [ ]; Slightly soluble [ ]; Of low solubility [ ]; Of very low solubility [ ]; Not soluble [ ]
Method:	Other
GLP:	Yes [ ] No [ ] ? [X]
Remarks:	This value represents the solubility of IPA without adjustment of pH. The pH of the water was not specifically stated though the pH of distilled water is typically between 6.0 and 7.0 depending on the amount of dissolved gas.
Reference:	Bemis et al., 1982

2.7 FLASH POINT *(liquids)*

(a)

Value:	
Type of test:	Closed cup [ ]; Open cup []; Other [ ]
Method:	Other
GLP:	Yes [ ] No [ ] ? []
Remarks:	
Reference:	

2.8 AUTO FLAMMABILITY *(solid/gases)*

(a)
Value:
Pressure:
Method:
GLP: Yes [ ] No [ ] ? [ ]
Remarks:
Reference:

2.9 FLAMMABILITY

Results: Extremely flammable [ ]; Extremely flammable - liquefied gas [ ]; Highly Flammable [ ]; Flammable [ ]; Non flammable [ ]; Spontaneously flammable in air [ ]; Contact with water liberates highly flammable gases [ ]; Other [ ]
Method:
GLP: Yes [ ] No [ ] ? [ ]
Remarks:
Reference:

2.10 EXPLOSIVE PROPERTIES

Results: Explosive under influence of a flame[ ];
More sensitive to friction than m-dinitrobenzene [ ];
More sensitive to shock than m-dinitrobenzene [ ]; Not explosive [ ];
Other [ ]
Method: Other
GLP: Yes [ ] No [ ] ? [ ]
Remarks:
Reference:

2.11 OXIDIZING PROPERTIES

Results: Maximum burning rate equal or higher than reference mixture [ ];
Vigorous reaction in preliminary test [ ];
No oxidizing properties [ ]; Other [ ]
Method: Other
GLP: Yes [ ] No [ ] ? [ ]
Remarks:
Reference:

2.12 ADDITIONAL REMARKS

Remarks: No additional remarks

2.13 ADDITIONAL DATA

A. Partition co-efficient between soil/sediment and water (Kd)

Value:
Method:
GLP:
Remarks: No studies located

Reference:

B. Other data

Results: No studies located
Remarks:
Reference:

3. ENVIRONMENTAL FATE AND PATHWAYS

3.1 STABILITY

3.1.1 PHOTODEGRADATION

(a)
Type: Air [X]; Water [ ]; Soil [ ]; Other [ ]
Light source: Sun light [ ]; Xenon lamp [ ]; Other [ ]
Light spectrum:
Relative intensity:
Concentration of Substance:
Temperature:
Direct photolysis:
Half life: 8.2 days
Degradation:
Quantum yield:
Method: calculated [x]; measured [ ]
Other
GLP: Yes [ ] No [x] ? [ ]
Test substance:
Remarks:
Result: Reaction rate constant with hydroxyl radicals=1.3×10^{-12} cm^3/mol-sec
Reference: AOPWIN (SRC, 2001)

3.1.2 STABILITY IN WATER

Type:
Half life:
Degradation:
GLP: Yes [ ] No [ ] ? [ ]
Test substance:
Remarks: Based on its chemical structure, isophthalic acid is not expected to undergo abiotic hydrolysis in the environment.
Reference:

3.1.3 STABILITY IN SOIL

(a)
Type: Field trial [ ]; Laboratory [ ]; Other [ ]
Radiolabel: Yes [ ] No [ ] ? [ ]
Concentration:
Soil temperature:
Soil humidity:
Soil classification: DIN19863 [ ]; NF X31-107 [ ]; USDA [ ]; Other [ ]
Year:
Content of clay etc.:
Organic Carbon:
Soil pH:
Cation exchange capacity:
Microbial biomass:
Dissipation time: DT 50:

DT 90:

Method:
GLP: Yes [ ] No [ ] ? [ ]
Test substance:
Remarks:
Reference:

3.2 MONITORING DATA (ENVIRONMENT)

Type of Measurement: Ambient annual average concentration
Media: Airborne Particulates
Results: 2.1, 3.4, 2.9 and 2.1 ng/m3
Remarks : Samples collected from west Los Angeles, downtown Los Angeles, Pasadena, and Rubidouc for 1982
Reference: Rogge WF et al. 1993. Atmos Environ 27A:1309-30

Type of Measurement: ..... Background concentrations
Media: Air
Results: A study was performed of the long-term transport of air pollution from large emission sources along the coastal areas in Japan to inland mountains. The resulting mean concentrations of IPA in airborne aerosols in a plume at Takasaki (July 26-31, 1986) and Karuizawa (July 29-31, 1986) were 2.2 and 1.3 ng/m^3, respectively. The ratio of carboxylic acids to acetylene (which is believed to be derived from the same sources) increased during the day and decreased at night and averaged 72% at Takasaki and 84% at Karuizawa. The authors proposed that IPA is almost entirely formed photochemically during long-term transport of airborne aerosols.
Reference: Satsumabayashi et al. (1990). Atmos, Environ. 24A: 1443-50

3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type: Adsorption [ ]: Desorption [ ]; Volatility [ ]: Other [ ]
Media:
Method:
Remarks:
Reference:

3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

Media: Air-biota [ ]; Air-biota-sediment-soil-water [x]; Soil-biota [ ]; Water-air [ ]; Water-biota [ ]; Water-soil [ ]; Other [ ]
Method: Fugacity level I [x]; Fugacity level II [x]; Fugacity level III [x]; Fugacity level IV [ ]; Other (calculation) [ ]; Other (measurement)[ ]
Results:

Media	Level I	Level II	Level III
Air	0.000090%	0.000090%	0.000013%
Water	99.9995%	99.9995%	76.1%

Soil	0.00041%	0.00041%	23.8%
Sediment	0.000009%	0.000009%	0.03%

Remarks: Predicted concentrations are not provided since default release estimates were used.
Reference: Trent University. 1991. Fugacity-based Environmental Equilibrium Partitioning Model. Version 2.17. Environmental Modeling Centre, Trent University, Peterborough, Ontario.

3.4 IDENTIFICATION OF MAIN MODE OF DEGRADABILITY IN ACTUAL USE

Results:
Remarks:
Reference:

3.5 BIODEGRADATION

(a)
Type: aerobic [X]; anaerobic [ ]
Inoculum: adapted [ ]; non-adapted [ ]; ? [ ]; sewage [X]
Concentration: 10.17 mg/l related to COD [ ]; DOC [ ]; Test substance [ ];
Medium: water [ ]; water-sediment [ ]; soil [ ]; sewage treatment [ ]
Degradation: >60% within 7 days
Results: Readily biodeg. [X]; Inherently biodeg. [ ]; under test condition no biodegradation observed [ ], Other [ ]
Method: OECD Guideline 301 B, Modified Sturm-Test
GLP: Yes [X] No [ ] ? [ ]
Test substance: Isophthalic Acid
Remarks: From the data obtained in the test, the test substance may be regarded as "readily biodegradable".
Reference: Battelle Europe, 1991

3.6 BOD_5,COD OR RATIO BOD_5/COD

BOD_5
Method:
Concentration:
Value:
GLP: Yes [ ] No [ ] ? [ ]

COD
Method: Other
Value:
GLP: Yes [ ] No [ ] ? [ ]

Ratio BOD_5/COD:

Remarks:
Result:
Reference:

3.7 BIOACCUMULATION

Species:	
Exposure period:	
Temperature:	
Concentration:	
BCF:	2
Elimination:	
Method:	Estimation
Type of test:	
GLP:	Yes [ ] No [x] ? [ ]
Test substance:	
Remarks:	
Reference:	Lyman W.J. et. al. Handbook of Chemical Property Estimation Methods. Chap 5,15 (1982)

3.8 ADDITIONAL REMARKS

A. Sewage Treatment

Remarks: No additional remarks

B. **Other**

Remarks:

4. ECOTOXICOLOGICAL DATA

4.1 ACUTE/PROLONGED TOXICITY TO FISH

(a)

Type of test:	static [X]; semi-static [ ]; flow-through [ ]; other [ ]; open-system [ ]; closed-system [ ]
Species:	*Leuciscus idus melanotus*
Exposure period:	96 hours
Results:	Based on nominal concentrations: LC_0 (96 hr): >1000 mg/L IPA and Isophthalic Sodium Salt (ISS) LC_{50} (96 hr): could not be determined NOEC (96 hr): = 1000 mg/L IPA and ISS Based on the measured average concentration of the highest concentration level tested: NOEC (96 hr): > 895 mg/L IPA and ISS
Analytical monitoring:	Yes [X] No [ ] ? [ ]
Method:	OECD Guideline No. 203 "Fish, Acute Toxicity Test"
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	Isophthalic Acid (Purity 99.9%)
Remarks:	The authors commented that IPA was ionized under test conditions. Therefore, it was believed that under test conditions and after pH adjustment, IPA and Isophthalic Sodium Salt were test materials investigated in this study.
Reference:	Battelle Europe, 1993.

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

A. Daphnia

(a)

Type of test:	static [x]; semi-static [ ]; flow-through [ ]; other [ ]; open-system [ ]; closed-system [ ]
Species:	*Daphnia magna* (Straus)
Exposure period:	48 hours
Results:	Based on nominal concentrations: EC_0: 1000 mg/L IPA and Isophthalic Sodium Salt (ISS) EC_{50}: could not be determined NOEC: = 1000 mg/L IPA and ISS Based on measured average concentration of the highest concentration tested: EC_0 >876 mg/L IPA and isophthalic sodium salt
Analytical monitoring:	Yes [X] No [ ] ? [ ]
Method:	OECD Guideline 202, Part I, 1984.
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	Isophthalic Acid (Purity 99.9%)
Remarks:	The authors commented that IPA was ionized under test conditions. Therefore, it was believed that under test conditions and after pH adjustment, IPA and Isophthalic Sodium Salt were test materials investigated in this study.
Reference:	Battelle Europe, 1993.

4.3 TOXICITY TO AQUATIC PLANTS e.g. Algae

(a)

Species:	Algae (*Scenedesmus subspicatus*)
End-point:	Biomass [ ]; Growth rate [X]; Other [ ]
Exposure period:	96 hour
Results:	Based on nominal concentrations: NOEC= 1000 mg/L IPA and Isopthalic Sodium Salt. Based on the measured average concentration of the highest concentration level tested: NOEC= 969 mg/L IPA and Isophthalic Sodium Salt.
Analytical monitoring:	Yes [X] No [ ] ? [X]
Method:	OECD No. 201 "Alga, Growth Inhibition Test"
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	Isophthalic Acid (purity 99.9%)
Remarks:	The authors commented that IPA was ionized under test conditions. Therefore, it was believed that under test conditions and after pH adjustment, IPA and Isophthalic Sodium Salt were test materials investigated in this study.
Reference:	Battelle Europe, 1993.

4.4 TOXICITY TO BACTERIA

(a)

Type:	Aquatic [ ]; Field [ ]; Soil [ ]; Other [X]
Species:	activated sludge
Exposure Period:	3 hr.
Results:	EC_5: 158.3 mg/L EC_{25}: 353.3 mg/L EC_{50}: 617.1 mg/L EC_{75}: 1077.9 mg/L EC_{95}: 2405.4 mg/l
Analytical monitoring:	Yes [ ] No [ ] ? [X]
Method:	OECD-Test Guideline 209: "Activated Sludge, Respiration Inhibition Test"
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	Isophthalic Acid (99.9% pure)
Test Condition:	Activated sludge was added to the test solution and was aerated with compressed air for 3 hr. After the contact time, the solutions were poured into an oxygen-bottle and oxygen consumption was recorded for 10 minutes to determine respiration rates.
Reference:	Batelle Europe, 1991

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4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS

4.5.1. CHRONIC TOXICITY TO FISH

No studies located

4.5.2. CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

No studies located

4.6 TOXICITY TO TERRESTRIAL ORGANISMS

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

No studies located

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Type of test:	Growth inhibition
Species:	Rice seedlings
Results:	Concentrations of 10 or 100 ppm had slight to no inhibition on plant growth
Remarks:	Inadequate detail to assess overall quality therefore not included in SIAR.
Reference:	Isogai et al. 1972. SCI PAP COLL GEN EDUC, UNIV TOKYO 22 (2): 129

4.6.3 TOXICITY TO OTHER NON MAMMALIAN TERRESTRIAL SPECIES (INCLUDING AVIAN)

No studies located

4.7 BIOLOGICAL EFFECTS MONITORING (INCLUDING BIOMAGNIFICATION)

Results: No studies located

4.8 BIOTRANSFORMATION AND KINETICS

No studies located

4.9 ADDITIONAL REMARKS

No additional remarks

5. TOXICITY

5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

(a)

Type:	LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain:	Sprague-Dawley rats
Value:	>5 g/kg
Method:	
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	isophthalic acid
Remarks:	Ten rats (5 male and 5 female) were administered 5 g/kg body weight IPA at a dosing volume of 15 ml/kg. Mean body weights increased during the study and gross necropsy findings were within normal limits for all animals. No deaths occurred during the study. Therefore, the median acute lethal oral dose of IPA was determined to be greater than 5 g/kg.
Reference:	IIT Research Institute, 1990.

(b)

Type:	LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain:	Albino Rat
Value:	13,000 mg/kg
Method:	
GLP:	Yes [ ] No [ ] ? [X]
Test substance:	isophthalic acid - 110
Remarks:	Ten rats (5 male and 5 female) were studied at each dose level. Rats were administered IPA in the form of either a 40% suspension in corn oil. A 95% confidence limit of 10,526-16,055 mg/kg was reported for the LD50. The authors concluded that IPA was practically non-toxic. Necropsy of the animals that died revealed pale, discolored kidneys.
Reference:	Industrial BIO-TEST Laboratories, Inc., 1975.

(c)

Type:	LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain:	Albino Rat
Value:	10,900 mg/kg
Method:	
GLP:	Yes [ ] No [ ] ? [X]
Test substance:	isophthalic acid - 85
Remarks:	Ten rats (5 male and 5 female) were studied at each dose level. Rats were administered IPA in the form of either a 40% suspension in corn oil. A 95% confidence limit of 8,862-13,407 mg/kg was reported for the LD50. The authors concluded that IPA was practically non-toxic. Necropsy of the animals that died revealed pale, discolored kidneys.
Reference:	Industrial BIO-TEST Laboratories, Inc., 1975.

(d)

Type	LD0 []; LD100 []; LD50 [X]; LD lo []; Other []
Species/strain:	Rat
Value:	12,200 mg/kg

Method:
GLP: Yes [] No [X] ? []
Test Substance: Isophthalic acid
Remarks: Ten rats (5 male, 5 female) were studies at each dose level. Rats were administered IPA in the form of either a 20% or 40% suspension in a 10% aqueous gum Arabic solution. Rats were monitored for 14 days. Mortality data were statistically analysed according to the method of Litchfield and Wilcoxon and the acute lethal dose was calculated. A 95% Confidence limit of 10.0 to 14.9 g/kg was reported for the LD50. Necropsy of the animals that died did not reveal any gross pathological alterations attributable to ingestion of test material.
Reference: Industrial BIO-TEST Laboratories, Inc 1958

(d)
Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain: Rat
Value: 10,400 mg/kg
Method:
GLP: Yes [ ] No [ ] ? [X]
Test substance: isophthalic acid
Remarks:
Reference: Marhold, 1986.

5.1.2 ACUTE INHALATION TOXICITY

a)
Type: LC_0 [ ]; LC_{100} [ ]; LC_{50} [ ]; LCL_0 [ ]; Other [X]
Species/strain: Albino Rats
Exposure time: 4 hours
Value: --
Method: Ten rats were exposed to11.37 g/m3 isophthalic acid (particle size: 1-5 microns). The animals were placed into specially designed chambers that were equipped with a Wright Dust Feed Mechanism which introduced the IPA in the form of a fine dust. The animals were exposed to the test material continuously for 4 hours. Observation of the animals after exposure was conducted for 16 days.
GLP: Yes [] No [ ] ? [X]
Test substance: isophthalic acid
Remarks: All test animals survived the acute inhalation exposures and were not observed to exhibit any adverse reactions during or after exposure.
Reference: Industrial BIO-Test Laboratories, Inc., 1958

5.1.3 ACUTE DERMAL TOXICITY

(a)
Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [ ]; LDL_0 [ ]; Other [ ]
Species/strain: Rabbits (New Zealand albino)
Value: >2,000 mg/kg body weight
Method: Single dose applied to the clipped back of each animal for 24 hours.
GLP: Yes [X] No [ ] ? [ ]
Test substance: Isophthalic Acid
Remarks: 5 male and 5 female rabbits received a single dermal dose of 2,000 mg/kg, applied for 24 hours. Animals were observed for 14 days following exposure.

No deaths were observed during the study. The authors concluded that the acute dermal LD50 value for IPA exceeds 2,000 mg/kg. Mild dermal irritation was observed in four animals immediately following unwrapping. No adverse treatment-related clinical signs were observed and no gross pathological lesions due to treatment were evident in any of the animals at necropsy. Mean body weights increased during the study.

Reference: ITTRI, 1990

(b)

Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [ ]; LDL_0 [ ]; Other [X]
Species/strain: Albino Rabbits
Value: The acute mean lethal dose is greater than 23,000 mg/kg
Method:
GLP: Yes [ ] No [ ] ? [X]
Test substance: isophthalic acid
Remarks: Rabbits were clipped with electronic clippers 24 hours prior to testing. The test material was applied to the exposure sites in the form of an aqueous paste. The exposure sites were covered with an impervious plastic sheeting that was firmly taped to the animal. Four animals at each of the four dose levels (4000, 8000, 16000, and 23000 mg/kg) were tested.
Reference: Industrial BIO-TEST Laboratories, Inc., 1958

5.1.4 ACUTE TOXICITY, OTHER ROUTES OF ADMINISTRATION

(a)

Type: LC_0 [ ]; LC_{100} [ ]; LC_{50} [ ]; LCL_0 [ ]; Other [ ]
LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain: Charles River Albino Rats
Route of Administration: i.m. [ ]; i.p. [X]; i.v. [ ]; infusion [ ]; s.c. [ ]; other [ ]
Exposure time:
Value: 13,000 mg/kg
Method:
GLP: Yes [ ] No [ ] ? [X]
Test substance: Isophthalic Acid-110
Remarks: 95% Confidence Limits of LD50 = 10,526 –16,055
Reference: Calandra, 1975

(b)

Type: LC_0 [ ]; LC_{100} [ ]; LC_{50} [ ]; LCL_0 [ ]; Other [ ]
LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain: mouse
Route of Administration: i.m. [ ]; i.p. [X]; i.v. [ ]; infusion [ ]; s.c. [ ]; other [ ]
Value: 4200 mg/kg
GLP: Yes [ ] No [ ] ? [X]
Test substance: Isophthalic Acid-110
Remarks:
Reference: Academie des Sciences, 1835-1965.

5.2 CORROSIVENESS/IRRITATION

5.2.1 SKIN IRRITATION/CORROSION

(a)

Species/strain: Rabbits (New Zealand white rabbits)

Results: Highly corrosive [ ]; Corrosive [ ]; Highly irritating [ ]; Irritating [ ]; Moderate irritating [ ]; Slightly irritating [ ]; Not irritating [X]

Method: A 500 mg dose of undiluted IPA was applied to skin that was previously clipped. The treated site was covered by adhesive dressing and the entire midsection of the rabbit was wrapped in a lint-free cloth towel and secured by an adhesive bandage.

GLP: Yes [X] No [ ] ? [ ]

Test substance: Isophthalic Acid

Remarks: The irritation score was 0.0/8.0 at all time points following unwrapping. The Primary Dermal Irritation Score for IPA was 0.0. No signs of dermal irritation or corrosivity were seen.

Reference: IITRI, 1990.

(b)

Species/strain: Rabbits (albino)

Results: Highly corrosive [ ]; Corrosive [ ]; Highly irritating [ ]; Irritating [ ]; Moderate irritating [ ]; Slightly irritating [ ]; Not irritating [X]

Method: A 500 mg dose of undiluted IPA was applied for 24 hours to abraded or unabraded skin that was previously clipped. The treated site was occluded.

GLP: Yes [ ] No [ ] ? [X]

Test substance: Isophthalic Acid

Remarks: With intact skin, mild erythema was noted in 1/6 animals at 24 hours (score=0.2/8), and 0/6 animals at 72 hours (score=0/8). With abraded skin, mild erythema was noted in 3/6 animals at 24 hours (score=0.5/8) and 0/6 animals at 72 hours (score=0/8). No edema was observed. The authors concluded that IPA is not an irritant.

Reference: Industrial Bio-Test Laboratories, 1975.

(c)

Species/strain: Rabbits (albino)

Results: Highly corrosive [ ]; Corrosive [ ]; Highly irritating [ ]; Irritating [ ]; Moderate irritating [ ]; Slightly irritating [ ]; Not irritating [X]

Method: A 500 mg dose of undiluted IPA was applied for 24 hours to abraded or unabraded skin that was previously clipped. The treated site was occluded.

GLP: Yes [ ] No [ ] ? [X]

Test substance: Isophthalic Acid

Remarks: With intact skin, mild erythema was noted in 1/6 animals at 24 hours (score=0.3/8), and 0/6 animals at 72 hours (score=0/8). With abraded skin, mild erythema was noted in 3/6 animals at 24 hours (score=0.7/8) and 3/6 animals at 72 hours (score=0.5/8). No edema was observed. The authors concluded that IPA is not an irritant.

Reference: Industrial Bio-Test Laboratories, 1975.

5.2.2 EYE IRRITATION/CORROSION

(a)

Species/strain: New Zealand Albino Rabbit

Results: Highly corrosive [ ]; Corrosive [ ]; Highly irritating [];

Irritating [ ]; Moderate irritating [ ]; Slightly irritating [X];
Not irritating [ ]

Classification: Irritating []; Not irritating [ ]; Risk of serious damage to eyes [ ]

Method: 100 mg of IPA was instilled into an eye of 6 rabbits. Irritation scores were recorded at 1, 2, 3, 4, 7 and 14 days following test article application.

GLP: Yes [X] No [ ] ? [ ]

Test substance: isophthalic acid-99

Remarks: The maximum irritation score of 5.3/110.0 was obtained 1 day after administration of the test article. Ocular irritation was seen in all rabbits during the study, but only three rabbits exhibited positive reactions. Complete recovery from all signs of ocular irritation was evident in two rabbits by the 2nd day, in five rabbits by the 4th day, and in all rabbits by the final scoring interval.

Reference: IIT Research Institute, 1985.

(b)

Species/strain: New Zealand Albino Rabbit

Results: Highly corrosive [ ]; Corrosive [ ]; Highly irritating [];
Irritating [ ]; Moderate irritating [ ]; Slightly irritating [X];
Not irritating [ ]

Classification: Irritating []; Not irritating [ ]; Risk of serious damage to eyes [ ]

Method: 100 mg of IPA was instilled into an eye of 6 rabbits. Irritation scores were recorded at 1, 24, 48, 72, and 168 hours.

GLP: Yes [ ] No [ ] ? [X]

Test substance: isophthalic acid-85

Remarks: An irritation score of 26.7/110 was reported at 1 hour, which diminished to 13.1/110 at 24 hours. Signs of irritation were completed resolved at 48 hours through 1 week. The authors concluded that IPA is not an eye irritant.

Reference: Industrial BIO-TEST Laboratories, Inc., 1975.

(c)

Species/strain: New Zealand Albino Rabbit

Results: Highly corrosive [ ]; Corrosive [ ]; Highly irritating [];
Irritating [ ]; Moderate irritating [ ]; Slightly irritating [X];
Not irritating [ ]

Classification: Irritating []; Not irritating [ ]; Risk of serious damage to eyes [ ]

Method: 100 mg of IPA was instilled into an eye of 6 rabbits. Irritation scores were recorded at 1, 24, 48, 72, and 168 hours.

GLP: Yes [ ] No [ ] ? [X]

Test substance: isophthalic acid-110

Remarks: An irritation score of 19/110 was reported at 1 hour, which increased slightly to 25.6/110 at 24 hours. Signs of irritation were completed resolved at 48 hours through 1 week. The authors concluded that IPA is not an eye irritant.

Reference: Industrial BIO-TEST Laboratories, Inc., 1975.

(d)

Species/strain: rabbit

Results: Highly corrosive [ ]; Corrosive [ ]; Highly irritating [];
Irritating [ ]; Moderate irritating [ ]; Slightly irritating [ ];
Not irritating [ ]

Classification: Irritating []; Not irritating [ ]; Risk of serious damage to eyes [ ]

Method: Standard Draize Test

GLP: Yes [ ] No [ ] ? [X]

Test substance: isophthalic acid
Remarks: Mild reaction
Reference: Prehled Prumyslove Toxikologie, 1986.

5.3 SENSITISATION

(a)
Type: Dermal Sensitzation
Species/strain: Guinea Pig
Results: Sensitizing [ ]; Not sensitizing [X]; ambiguous [ ]
Number of animals with respective erythema scores

Group	Induction										Challenge									
	24 hours					48 hours					24 hours					48 hours				
	Erythema Score					Erythema Score					Erythema Score					Erythema Score				
	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4
Treated		9	1			6	4				2	7	1			3	7			
Vehicle control	1	3	6			2	3	3			3	7				8	2			
Sham Control	10					10					3	7				4	6			

Classification: Sensitizing [ ]; Not sensitizing [ ]

Method: Modified Buehler Method. A dose of 0.3 mL of a 30% solution of IPA in dimethyl sulfoxide (DMSO) was applied to the shaved backs of 10 male guinea pigs once a week for 3 weeks during the induction period. The 30% solution was the maximum concentration to cause mild irritation (Driaze score of 2 or less). Another group of 10 guinea pigs served as a vehicle control and was similarly dosed with 0.3 ml of undiluted DMSO. A third group of 10 sham control animals was handled in the same way but was not treated with vehicle or test article. Two weeks following the last induction dose, the treated and sham control animals received a challenge dose of 0.3 mL of a 30% solution of IPA; the vehicle control received a 0.3 ml of a 70% aqueous DMSO solution.. Using a body weight of 0.6 kg, the treatment corresponds to a dose of approximately 15,000 mg/kg.

GLP: Yes [X] No [ ] ? [ ]

Test substance: isophthalic acid

Remarks: A positive erythema response (score> or = 2) was elicited in 1/10 animals. The primary effect of treatment (treated vs. control) and the secondary effect of time of scoring (24 vs 48 hours) were not statistically significant. The authors concluded that IPA is not a dermal sensitizer. The same concentration (30%) was used for both the induction and challenge phase which represents a slight deviation from standard protocol. However, because conditions were more stringent and results were still negative it is not believed to affect the conclusion.

Reference: IIT Research Institute, 1991.

5.4 REPEATED DOSE TOXICITY

(a)

Species/strain: rats (Wistar-derived stock)

Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]

Route of Administration: oral

Exposure period: 13 weeks

Frequency of treatment: once/day

Post exposure observation period:

Dose: 0.5, 1.6, 5.0% of a normal diet (250, 800, 2500 mg/kg/day)

Control group: Yes [X]; No [ ]; No data [ ];
Concurrent no treatment [ ]; Concurrent vehicle [X]; Historical [ ]

NOEL: 0.5% (approximately 250 mg/kg-day)

LOEL: 1.6% (approximately 800 mg/kg-day)

Method: subchronic feeding study

GLP: Yes [ ] No [ ] ? [ ]

Test substance: Isophthalic Acid

Remark: Following the first week of the study, the weight gains of the rats were examined. It was concluded that the 5% dose level would not permit growth

or even survival of the animals. Therefore, the doses were reduced to 3%. Levels of 1.6% (approximately 800 mg/kg-day) in feed produced small increases in the incidence of crystalluria (1/25 males, 2/25 females) and renal pathology (5/25 males). This study identifies a NOAEL and LOAEL of 250 and 800 mg/kg-day, respectively, based on kidney effects in rats.

Reference: Vogin, 1972

(b)

Species/strain: Wistar and CD Rats

Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]

Route of Administration: dietary

Exposure period: 90 day

Frequency of treatment: once per day

Post exposure observation period:

Dose: 0, 0.03, 0.125, 0.5, 2.0, or 5% teraphthalic acid

Control group: Yes [X]; No [ ]; No data [ ];
Concurrent no treatment [ ]; Concurrent vehicle [X]; Historical [ ]

NOEL:

LOEL:

Method:

GLP: Yes [ ] No [ ] ? [X]

Test substance: Teraphthalic Acid, an isomer of IPA

Remark: Dose-related decreases in food consumption, body weight, and weight gain were found in both male and female Wistar and CD rats. Statistically significant decreases were confined mainly to the two highest dietary levels of TPA.

Reference: Gibson, 1982

(c)

Species/strain: Sprague-Dawley rats

Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]

Route of Administration: inhalation

Exposure period: 4 weeks

Frequency of treatment: 6 hours/day, 5 days/week

Post exposure observation period:
3 weeks (5 rats/sex/group in the control group and the high dose level groups designated for pre-exposure, single exposure, and weekly serum analysis)

Dose: 1.0, 5.0, and 10.0 mg/m3

Control group: Yes [X]; No [ ]; No data [ ];
Concurrent no treatment [ ]; Concurrent vehicle [X]; Historical [ ]

NOEL: 10 mg/m3

LOEL: --

Method: subchronic inhalation of particulate aerosol

GLP: Yes [ ] No [ ] ? [X]

Test substance: isophthalic acid

Remark: The dosing groups contained 10 male and 10 female rats each. In addition, 5 rats/sex were designated for pre-exposure, single exposure, and weekly serum analysis. These rats were included in the control group and the high exposure groups. There were no statistically significant effects of treatment on any body weight or organ weights in the exposed rats. In addition, there were no significant differences in hematology or clinical chemistry parameters between the exposed groups and control group.

Reference: IIT Research Institute, 1988.

5.5 GENETIC TOXICITY IN VITRO

A. BACTERIAL IN VITRO TEST

(a)

Type: Mutagenicity, Bacterial Reverse Mutation Assay
System of testing: *Salmonella typhimurium* (TA 1535, TA 1537, TA 1538, TA 98, and TA 100)
Concentration: 5, 50, 500, or 5000 ug/plate
Metabolic activation: With [ ]; Without [ ]; With and Without [X]; No data [ ]
Results:
Cytotoxicity conc:
Precipitation conc: --
Genotoxic effects:

	+	?	--
With metabolic activation:	[ ]	[ ]	[X]
Without metabolic activation:	[ ]	[ ]	[X]

Method: Salmonella/Mammalian-Microsome Reverse Mutation Test (OECD 471)
GLP: Yes [X] No [ ] ? [ ]
Test substance: Isophthalic Acid 220
Remarks: Isophthalic acid 220 showed no evidence of mutagenic activity when tested in this bacterial system.
Reference: Huntingdon Research Centre, 1991

(b)

Type: Mutagenicity/ Bacterial Reverse Mutation Assay
System of testing: *Salmonella typhimurium* (TA98, TA100, TA1535, TA1538)
Concentration: 0, 667, 1000, 3333, 6667, or 10000 ug/plate
Metabolic activation: With [ ]; Without [ ]; With and Without [X]; No data [ ]
Results:
Cytotoxicity conc:
Precipitation conc:
Genotoxic effects:

	+	?	--
With metabolic activation:	[X]	[ ]	[ ]
Without metabolic activation:	[X]	[ ]	[ ]

Method: Salmonella/Mammalian-Microsome Reverse Mutation Test (OECD 471)
GLP: Yes [X] No [ ] ? [ ]
Test substance: Isophthalic Acid
Remarks: Under the conditions of this assay, IPA did cause reproducible positive responses in various strains in the presence and absence of microsomal enzymes.
Reference: Microbiological Associates, Inc. 1990.

(c)

Type: Mutagenicity/ Bacterial Reverse Mutation Assay
System of testing: *Salmonella typhimurium* (TA 98, TA 100, TA 1535, TA 1537, and TA 1538)
Concentration: 0, 4, 20, 100, 500, 2500, and 10000 ug/plate
Metabolic activation: With [ ]; Without [ ]; With and Without [X]; No data [ ]
Results:
Cytotoxicity conc:
Precipitation conc: --
Genotoxic effects:

	+	?	--
With metabolic activation:	[X]	[ ]	[ ]

	Without metabolic activation: [X] [ ] [ ]
Method:	Salmonella/Mammalian-Microsome Reverse Mutation Test (OECD 471)
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	Isophthalic Acid
Remarks:	Isophthalic acid was found to be not toxic to the bacterial strains. The test compound was found to be mutagenic with and without exogenous metabolic activation.
Reference:	Muller, 1991.

B. NON-BACTERIAL IN VITRO TEST

(a)

Type:	Chromosomal Aberration
System of testing:	Chinese hamster ovary cells
Concentration:	625, 1250, 2500, and 5000 ug/ml
Metabolic activation:	With [ ]; Without [ ]; With and Without [X]; No data [ ]
Results:	
Cytotoxicity conc:	--
Precipitation conc:	--
Genotoxic effects:	+ ? --
	Without metabolic activation: [ ] [ ] [X]
Method:	OECD 473
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	Isophthalic Acid
Remarks:	No increase in chromosome aberrations was observed in either the non-activated or S-9 activated test system. IPA was concluded to be negative in the cytogenetics assay.
Reference:	Microbiological Associates, Inc.1991.

(b)

Type:	Mammalian Cell Gene Mutation/HGPRT Mutation Assay
System of testing:	Chinese hamster ovary cells
Concentration:	125, 250, 500, 1500, 2000, and 3000 ug/ml (non-activated); 250, 500, 1000, 1500, 2000, and 3000 ug/ml (activated).
Metabolic activation:	With [ ]; Without [ ]; With and Without [X]; No data [ ]
Results:	
Cytotoxicity conc:	
Precipitation conc:	--
Genotoxic effects:	+ ? --
	Without metabolic activation: [ ] [ ] [X]
	With metabolic activation: [ ] [ ] [X]
Method:	OECD 476
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	Isophthalic Acid
Remarks:	Isophthalic acid was found to be negative in the CHO/HGPRT mutation assay both in the absence and presence of exogenous metabolic activation.
Reference:	Microbiological Associates, 1991

(c)

Type:	Mammalian Cell Gene Mutation/Lymphoma Assay
System of testing:	Mouse lymphoma L5178Y cells
Concentration:	150, 300, 450, 600, 650, 700, 750, 800, 850, 900 and 950 ug/ml.
Metabolic activation:	With [ ]; Without [ ]; With and Without [X]; No data [ ]

Results:
Cytotoxicity conc:
Precipitation conc: --
Genotoxic effects: + ? --
Without metabolic activation: [ ] [ ] [X]
With metabolic activation: [ ] [ ] [X]
Method: Mouse Lymphoma Mutation Assay (OECD 476)
GLP: Yes [X] No [ ] ? [ ]
Test substance: Isophthalic Acid
Remarks: Based on the results of this study, there is no conclusive evidence of mutagenic activity attributable to isophthalic acid in mouse lymphoma cells.
Reference: Riach and Willington, 1994.

5.6 GENETIC TOXICITY IN VIVO

(a)
Type: Micronuclei Formation
Species: Mouse
Strain: ICR
Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
Concentration: 200, 400, 800 mg/kg
Route of Administration: i.p.
Frequency of treatment: once
Sampling frequency: once, 24 hours post-exposure
Results: Negative. Mortality was observed in 1/15 male mice that had been treated with 800 mg/kg TPA. One mouse from the replacement group was used in place of the animal that died. Clinical signs following treatment with either dose of TPA included lethargy and piloerection. Negative and positive control animals appeared normal during the course of the study. The total number of micronuclei observed per 20000 PCE in animals treated with vehicle, 200, 400 or 800 mg/kg for 24 hours was 4, 8, 5, and 4, respectively. The incidence of micronuclei in animals treated with 800 mg/kg also did not differ from the vehicle control at 48 hours (2/20000 vs. 8/20000, respectively). There was no difference between males and females. TPA was negative in the test. The test was valid, as the incidence of micronuclei in the vehicle control was not greater than 5/1000 PCE and the number of micronucleated cells in the positive controls (382/20000) was significantly different ($p < 0.05$) from the vehicle control. Reductions (up to 9%) in the ratio of polychromatic erythrocytes to total erythrocytes were observed in some of the treated groups relative to the vehicle control, suggesting that the test article did not inhibit erythropoiesis. Greater reductions in this ratio were observed in animals treated with cyclophosphamide (25-29%).
Toxic concentration: 800 mg/kg
Remarks: Criteria for a valid test: The mean incidence of micronucleated polychromatic erythrocytes must not exceed 5/1000 polychromatic erythrocytes (0.5%) in the negative control vehicle. The incidence rate in the positive control group must be significantly increased relative to the negative control ($p<0.05$, Kastenbaum-Bowman Tables).
Method: OECD 474
GLP: Yes [X] No [ ] ? [ ]
Test substance: Terephthalic acid (an isomer of IPA)
Reference: Bioreliance, 2001

5.7 CARCINOGENICITY

Although no data were located regarding the carcinogenicity of IPA, some information is available for its isomer, TPA.

(a)

Species:	Rat
Sex:	Male/female
Strain:	Fischer 344
Route of admin.:	Oral feed
Exposure period:	Lifetime (2 years)
Frequency of treatment:	Daily
Post. obs. period:	
Doses:	0, 20, 142, 1000 mg/kg/day
Control Group:	Yes, concurrent no treatment
Method:	Other
Year:	1983
GLP:	Unknown
Test substance:	TPA
Remark:	Terephthalic acid induced bladder stones were seen in 13/126 females in the high dose group. At the scheduled 6 and 12 month sacrifices, no bladder calculi were detected. At the 18 month sacrifice sand like particle or bladder calculi were only seen in two of the high dose females. There were 18/118 females with what was described as transitional cell adenomas by one pathology laboratory and epithelial hyperplasia by another. Two of these were detected in high dose females after 18 months (2/27), 15 were seen in seen in high dose females at the end of the study (15/79), and one was seen in a control female at the end of the study. None were found in the males, nor at any other dose level. It was believed that rats fed high concentrations of terephthalic acid in the diet develop bladder calculi which appear to cause chronic inflammation of the bladder epithelium, bladder hyperplasia and subsequently bladder tumours. An apparent threshold effect exists because animals exposed to lower concentrations for their lifetime do not form bladder calculi or tumors. The high dose group in this study (1000 mg/kg/day) corresponds to an approximate dietary concentration of 2.0% to 2.8% in adult Fisher rats.
Reference:	CIIT (1983) Chronic Dietary Administration of Terephthalic Acid. CIIT Docket 20124

(b)

Species:	Rat
Sex:	Male/female
Strain:	Wistar
Route of admin.:	Oral feed
Exposure period:	2 years
Frequency of treatment:	Daily
Post. obs. period:	
Doses:	1% (500 mg/kg/day) & 2% (1000 mg), 5% (2500 mg)
Control Group:	Unknown
Method:	
Year:	1974

GLP: Unknown
Test substance: As prescribed in 1.1 - 1.4
Remark: Reduced body weight gain occurred at in the 5% dose level (males and females) and in the 2% dose level (males). At 1%, reduced relative liver weight in females and reduced relative kidney size in males and females. At 2%, reduced liver, kidney, and heart weights (females only). At 5%, there was increased kidney weight in males, and increased adrenal weights in males and females; as well as increased mortality, mainly as a result of increased incidence of bladder stones (at 5%: males, 42/47; females, 39/42; at 1%: females, 1/48). There was increased incidence of bladder and ureter tumors (at 5%: males, 21/37; females, 21/34; at 2%: males, 1/48; females, 2/48; at 1%: males, 1/43.). There was increased incidence of bladder and ureter tumors.
Reference: Gross J. (1974) The effects of prolonged feeding of terephthalic acid (TPA) to rats. Project FG-IS-175. Submitted to US Dept. of Agriculture, Agriculture Research Service, Washington D.C.

(c)
Species: Mouse
Sex: Female
Strain: C3H
Route of admin.: Oral feed
Exposure period: 12 months
Frequency of treatment: Daily
Post. obs. period:
Doses: 5%
Control Group: Unknown
Method:
Year: 1973
GLP: Unknown
Test substance: No data
Remark: Reduced number of mammary tumours. At 12 months, mammary tumours occurred in 78% of controls and in 50% of treated mice.
Reference: Nagasawa H, Fujimoto M. (1973) Experimentia 29, 89. Cited in BIBRA Toxicity Profile
1995

5.8 TOXICITY TO REPRODUCTION

Although no data were located regarding the toxicity to reproduction of IPA, some information is available for its isomer, Terephthalic acid.

(a)
Type: Fertility [ ]; One generation study [X]; Two generation study [ ]; Other [ ]
Species/strain: Wistar and CD Rats
Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
Route of Administration: dietary
Exposure period: Parental: 90 days prior to breeding and throughout mating gestation, lactation, and postweaning periods, Offspring: 51 days birth through lactation, 30 days post-weaning
Frequency of treatment: *ad libitum*

Postexposure observation period:
Premating exposure period: male: 90 days female: 90 days
Duration of the test:

Doses:	diets containing 0, 0.03, 0.125, 0.5, 2.0, and 5.0% terephthalic acid (TPA)
Control group:	Yes [X]; No [ ]; No data [ ]; Concurrent no treatment [ ]; Concurrent vehicle [X]; Historical [ ]
NOEL Parental:	0.5% CD rats (approximately 240-282 mg/kg-day), 2.0% Wistar rats (approximately 960-1219 mg/kg-day)
LOEL Parental:	2.0% CD rats (approximately 930-1107 mg/kg-day), 5.0% Wistar rats (approximately 2480-3018 mg/kg-day)
NOEL F1 Offspring:	0.5% (both strains, approximately 240-307 mg/kg-day)
LOEL F1 Offspring:	2% (both strains, approximately 930-1219 mg/kg-day)
NOEL F2 Offspring:	--
LOEL F2 Offspring:	--
Results:	Parental Effects: Following 90 days of exposure to TPA, statistically significant decreases in food consumption were observed in CD females treated with 2% and 5%, and in both sexes of Wistars treated with 5%. Body weights were statistically decreased after 13 weeks in both sexes of CD rats on 2% and 5% TPA diets, and in males exposed to 0.03%. This effect occurred in Wistars (both sexes) only at the 5% level. There were 5 deaths (3 CD females, 1 Wistar/sex) reported during weeks 4-13 in animals given 5% TPA in the diet. During the one-generation component of the study 3 CD (1 male at 2.0%, 1/sex at 5.0%) and 4 Wistar female (2 at 5.0% and 2 at 0.03%) rats died. There was no effect of treatment on fertility index and litter size. Offspring Effects: There were no effects of treatment on litter size, sex ratio, or total number of offspring. While no control offspring were found dead on Day 0, 17 Wistar pups (1 at 0.03%, 2 at 0.125%, 1 at 0.5%, 12 at 2.0% (2 from one dam and 10 from another)) and 23 CD pups (1 at 0.5%, 7 at 2.0% (3 dams) and 15 at 5.0% (3 dams; with 11 from one of them)) were found dead. No statistical differences were noted in viability on Days 0, 1, or 21 in either strain. In CD rats, survivability on Day 21 was reduced in both sexes of offspring whose parents had been exposed to 5% TPA in the diet. In Wistar rats, body weights of both sexes of offspring from dams given 5.0% were reduced at Day 1. On Day 21, body weight was reduced in both strains of offspring from dams that ingested 5% TPA in the diet. Increased postnatal deaths on Day 1 and decreased survivability to Day 21 were noted in the 2% and 5% groups. At these dose levels, several large litters of pups were lost to dams suffering obvious signs of toxicity. Several of these dams did not allow the pups to nurse or attend to the litters. These pups were noted not to have milk in their stomachs and presented clinically as being very weak. These dams were consuming dietary levels of TPA known to cause reduced feed consumption, diarrhea and gastric trichobezoars (hairballs) and induce the formation of renal and bladder calculi. Unscheduled deaths during the postweaning period (Day 21-51) were confined to the 5% TPA group (18 Wistar and 16 CD) and were associated with a very high incidence of renal and bladder calculi. Renal and bladder calculi were noted in all animals exposed to 5% that were necropsied at Day 21. Day 51 necropsy findings also reported a very high incidence of renal and bladder calculi and the histological sequelae of the presence of the calculi.
Method:	One generation reproductive toxicity test
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	.....Terephthalic Acid (TPA), an isomer of IPA
Reference:	Gibson, 1982

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

(a)

Species/strain: Sprague-Dawley rats
Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
Route of Administration: inhalation
Duration of the test: 7 days/week , for a total of 10 consecutive exposures.
Exposure period: Gestation days 6 through 15
Frequency of treatment: 6 hours/day, 7 days/week
Doses: 0, 1.0. 5.0, and 10.0 mg/m3
Control group: Yes [X]; No [ ]; No data [ ];
Concurrent no treatment [ ]; Concurrent vehicle [X]; Historic al [ ]
NOEL Maternal Toxicity:
NOEL Fetotoxicity:
NOEL Teratogenicity -- >10 mg/m3
Results: Exposure to IPA during the major organogenesis period did not result in any significant toxic or teratogenic effects in the dam or fetus.
Method:
GLP: Yes [X] No [ ] ? [ ]
Test substance: isophthalic acid
Remarks: IPA was administered to four groups of 16-18 timed-pregnant primiparous rats. The incidences of clinical signs in the IPA-exposed rats and the control rats were similar. No deaths occurred during the study.
Reference: IIT Research Institute, 1991.

5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities

Type:
Results:
Remarks:
Reference:

B. Toxicodynamics, toxicokinetics

(a)

Type: Subchronic feeding study
Species/Strain Rat/Wistar
Results:
Remarks: Blood levels of IPA and TPA (determined as total mg phthalate/L) collected during a 13-week feeding study were increased in a dose-dependent manner on days 7, 30, 60, and 90. IPA and TPA levels were generally highest during the first week of exposure and declined during the course of the study, suggesting either a change in feed consumption rates or some sort of adaptation resulting in increased clearance of IPA. 24-Hour urinary excretion data collected on days 7, 30, 60, and 90 indicate that urinary excretion, presumably as unchanged chemical, is the primary mechanism by which IPA and TPA are eliminated from the body.
References: Vogin, E.E. 1972. Subacute feeding studies (13-week) in rats with

demethylterepthalate (DMT), isophthalic acid (IA), and terephthalic acid (TA). Food and Drug Research Laboratories, Incorporated, Laboratory No. 0411.

(b)
Type: Subchronic inhalation study
Species/Strain Rat/Wistar
Results:
Remarks: Blood levels of IPA were detected immediately following exposure in rats exposed to 10 mg/m^3 for 6 hours/day. Levels remained elevated during the exposure period. Serum concentrations detected in female rats (5.3-9.3 ug/mL) were consistently higher than the concentrations detected in male rats (1.4-3.4 ug/mL). The data suggest that steady state is achieved fairly rapidly (on the first day of exposure). One week following exposure, IPA was not detected in blood, indicating that clearance of IPA from the body occurs fairly rapidly. Based on a log Kow value of –2.34, IPA is not expected to accumulate appreciably in tissues, and is likely to be readily excreted from the body.
References: IITRI 1988

(c)
Type: Subchronic inhalation study
Species/Strain Rat/Sprague-Dawley
Results: Sprague-Dawley rats were exposed by inhalation to a particulate aerosol of 10 mg/m^3 terephthalic acid. Exposure was 6 hours per day for 25 consecutive days, followed by a 28-day post-exposure recovery period. Blood and urine samples were collected one day prior to exposure and after 1, 5, 10, 15, 25 days of exposure and every 7 days during the 28 day recovery period. Terephthalic acid was not detected in the blood after the first 5 days of exposure. Detectable blood concentrations of terephthalic acid were observed after 10 consecutive days of exposure and progressively increased over the remaining exposure period. The highest mean blood concentration was 2.7 ug/ml after 25 days. Seven days after completion of the exposure period, the blood concentration of terephthalic acid was less than 1 ug/ml. However, the presence of trace levels of terephthalic acid was detected in the blood throughout the post-exposure recovery period.
Reference: IIT Research Institute 1989. Time Course Analysis of Terephthalic Acid Concentration in Blood and Urine of Rats Following Inhalation Exposures. Study IITRI Study #1448A

5.11 EXPERIENCE WITH HUMAN EXPOSURE

(a)
Results:
Remarks:
Reference:

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Robust Study Summaries
ISOPHTHALIC ACID

.....

CAS No. 121-91-5

Sponsor Country: U.S.A.

DATE: January, 2002

PHYSICAL/CHEMICAL ELEMENTS

MELTING POINT

TEST SUBSTANCE
- Isophthalic Acid (IPA)

METHOD
- Method/guideline:
- GLP: ?
- Year (study performed):
- Remarks:

RESULTS
- Melting point: 347 °C
- Decomposition:
- Sublimation:
- Remarks:

CONCLUSIONS
- The melting point for IPA is 347 °C

DATA QUALITY

REMARK
- The CRC Handbook of Chemistry and Physics reference for the melting point was considered more reliable because it reported a specific melting point rather than a range, though all reported values were very similar.

REFERENCES
- Lide, D.R. (ed.) CRC Handbook of Chemistry and Physics. 75th ed. Boca Raton, Fl: CRC Press, Inc., 1994-1995. IN HSDB, 2001.

OTHER
- 345-348ºC Merck, 9th Edition; 314-343 ºC Aldrich.

BOILING POINT

TEST SUBSTANCE

- Isophthalic Acid (IPA)

METHOD

- Method:
- GLP: ?
- Year (study performed):
- Remarks:

RESULTS

- Boiling point: sublimes
- Pressure:
- Pressure unit:
- Decomposition (yes/no/ambiguous)
- Remarks:

CONCLUSIONS

- IPA has been found to sublime.

DATA QUALITY

REFERENCES

- Lide, D.R. (ed.) CRC Handbook of Chemistry and Physics. 75th ed. Boca Raton, Fl: CRC Press, Inc., 1994-1995. IN HSDB, 2001.

OTHER

VAPOUR PRESSURE

TEST SUBSTANCE

- Isophthalic Acid (IPA)
- Remarks:

METHOD

- Method:
- GLP: ?
- Year (study performed):
- Remarks:

RESULTS

- Vapor Pressure: 9 Pa (0.068 mm Hg)
- Temperature: 100 °C
- Decomposition:
- Remarks:

CONCLUSIONS

- The vapor pressure for IPA is 9 Pa at 100°C and is approximately 2.25 Pa at 25°C.

DATA QUALITY

REFERENCES

- Dauber, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989. IN HSDB, 2001.

OTHER

- Sublimation may have influenced the high-temperature measurement. The extrapolation from high temperature to environmentally relevant temperature (e.g. 25ºC) may be inaccurate.

VAPOUR PRESSURE

TEST SUBSTANCE
- Isophthalic Acid (IPA)
- Remarks:

METHOD
- Method: MPBPWIN version 1.40 (Model)
- GLP: No
- Year (study performed):
- Remarks:

RESULTS
- Vapor Pressure: 3.5×10^{-6} Pa (2.6×10^{-8} mm Hg)
- Temperature:
- Decomposition:
- Remarks: Modified Grain Method selected.

CONCLUSIONS
- The vapor pressure for IPA is estimated to be 3.5×10^{-6} Pa.

DATA QUALITY
- (2) Reliable with restrictions. Value is an estimate by an accepted method.

REFERENCES
- MPBPWIN version 1.40 (US EPA EPIWIN Suite Software)

OTHER
- Other QSAR estimates ranged from 1.57×10^{-7} mm Hg using the Mackay method to $1.19\ 10^{-8}$ mm Hg using the Antoine method. The Modified Grain method was selected by the software.
- Because the QSAR model provides estimates at the environmentally relevant temperature, it was preferred to the estimate derived by an extrapolation from a measurement at a high temperature.

PARTITION COEFFICIENT

TEST SUBSTANCE

- Isophthalic Acid (IPA)
- Remarks: Purity 99.9%

METHOD

- Method: OECD 107 "Partition Coefficient (n-octanol/water)"
- GLP: Yes
- Year (study performed): 1991
- Remarks: The water phase was buffered to pH 7 because of the possibility of ionization. Buffer was prepared by diluting 200 ml of 1M sodium hydroxide to 700 ml with water, adjusting to pH 7 with glacial acetic acid, and adjusting the final volume to one liter. Solvents (octanol and buffer) were presaturated by shaking at room temperature. Test sample was added to each of three test conditions consisting of varying ratios of octanol to buffered water. Solutions were mixed for 30 minute then centrifuged at 1500 rpm for 5 minutes to separate the two phases. Three replicate samples were prepared from each of three test conditions.

RESULTS

- Log P_{ow}: -2.34
- Temperature: 22°C
- Remarks: Chemical analyses conducted by high performance liquid chromatography (HPLC). Recoveries ranging from 92.6-98.1% were reported. The mean recovery was 95.4 percent. There was no trend in the partition coefficient with varying amounts of water.

CONCLUSIONS

- The Log Pow value for IPA is –2.34.

DATA QUALITY

- (1) Reliable without restrictions

REMARKS

- The Log Pow of the ionized form of isophthalic acid (value determined a pH 7) is believed to be the most relevant as this is the form most likely encountered in the environment.

REFERENCES

- ITT Research Institute. 1992. Determination of the Octanol/Water Partition Coefficient of Isophthalic Acid (IPA). Study No. 1705.

OTHER

- Log Pow: 1.66 (Hansch and Leo, 1981) This value may represent to Log Pow of the neutral form which w ould explain the difference between this value and the measured value above. In sufficient documentation of methods to assess. Log Pow 1.76 (KOWWIN in USEPA EPIWIN Suite software.

WATER SOLUBILITY

TEST SUBSTANCE

- Identity: Isophthalic Acid (IPA)

METHOD

- Method:
- GLP: ?
- Year (study performed):
- Remarks:

RESULTS

- Value: 0.013 g/100 g at 25°C
- Description of solubility:
- pH value and concentration at temperature °C:
- pKa value at 25 °C:
- Remarks: .

CONCLUSIONS

- The water solubility of IPA is 0.013 g/100 mL (130 mg/L).

DATA QUALITY

REFERENCES

- Bemis, A.G., Dindorf, J.A., Horwood, B., Samans, C. 1982 Phthalic acids and other benzenepolycarboxylic acids. In: Kirk-Othmer encycl. Chem Tech 3Rd Ed. 17: 732-77.

OTHER

- 40 mg/L at 1°C; 130 mg/L at 25°C; 300 mg/L at 50°C; 2400 mg/L at 100°C (Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed. Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984, p V17 759). Reported in HSDB 2001.

ENVIRONMENTAL FATE ELEMENTS AND PATHWAYS

PHOTODEGRADATION

TEST SUBSTANCE
- Isophthalic Acid

METHOD
- Method/guideline: Estimated - AOPWIN
- Type (test type): Estimated
- GLP:
- Year (study performed): 2001
- Remark: Assumptions molecular weight 166, water solubility 130 mg/L, vapor pressure 3.5 x 10^{-6} Pa at 25º C, Log Kow = -2.34.

RESULTS
- Direct photolysis:
- Half-life t ½ : 8.2 days
- Remarks: Overall OH Rate Constant: 1.3E-12 cm^3/molecule-sec at 25 degrees C, Concentration of OH radical is 1.5E 6 OH/cm^3, 12 hour day

CONCLUSIONS

DATA QUALITY
- (2) Reliable with restrictions. Value is an estimate by an accepted method.

REFERENCES
- SRC. 2001. Atmospheric Oxidation Program for Microsoft Windows (AOPWIN). Syracuse Research Center.

OTHER
- IPA in the vapor-phase is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 12.3 days (Meylan and Howard, 1993).

STABILITY IN WATER

TEST SUBSTANCE

METHOD

- Method/guideline:
- Type (test type):
- GLP:
- Year (study performed):
- Remarks:
- Duration:
- Positive Controls:
- Negative Controls:
- Analytical procedures:

RESULTS

- Measured value:
- Degradation:
- Breakdown products:
- Remarks: Based on the chemical structure, isophthalic acid is not expected to undergo abiotic hydrolysis in the environment.

CONCLUSIONS

DATA QUALITY

REFERENCES

OTHER

- IPA is biodegradable in screening tests (Japan Chemical Industry Report, 1992; Pitter, 1976), it may also biodegrade in water. The absorption of UV radiation >290 nm (Sadtler Research Lab, 19??) suggests that IPA may directly photodegrade in surface waters.

TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY)

TEST SUBSTANCE

- Isophthalic Acid

METHOD

- Test (test type): Calculated
- Method: Level I, II, and III Fugacity
- Year (study performed): 2001
- Remarks: Chemical Assumptions: Molecular weight=166 g/mol; water solubility=130 g/m^3; Vapor pressure=3.5 x 10^{-6} Pa; Log Kow=-2.34; Melting Point=347ºC; Temperature=25ºC; Half life in air=288 hr. Default values for release estimates were assumed for Level 1 (single release of 100,000 kg), Level 2 (continuous release of 1,000 kg/hr), and Level 3 (continuous release of 1,000 kg/hr each to air, water, and soil). All environmental parameters were default values.

RESULTS

- Media: Air, soil, water, and sediment concentrations

	Level I	Level II	Level III
Air	0.000090%	0.000090%	0.000013%
Water	99.9995%	99.9995%	76.1%
Soil	0.00041%	0.00041%	23.8%
Sediment	0.0000090%	0.0000090%	0.03%

- Remarks: Predicted concentrations are not provided since default release estimates were used. Ionization of IPA would increase the water solubility, but use of a higher water solubility (2300 mg/L) had no significant effect on predicted distributions.

- Remarks: IPA was modeled as a Type 1 chemical using the Trent University software, i.e., it was assumed capable of partitioning into all media. A more correct approach would have been to model IPA as a Type 2 chemical with a Z value of zero or near-zero in air, and an initial estimate of Z in water of 1.0. This partitioning model would be calculated using the equivalence approach instead of the fugacity calculation. However, the required partition coefficients for Type 2 models are not those used for Type 1 chemicals, and were not available. In the absence of data, errors and uncertainties from using estimated parameters would be likely to counteract any improved accuracy from using a better model. The fugacity model did indicate zero or near-zero amounts in air. Consequently, more detailed modeling would be unlikely to significantly affect the prediction of environmental distribution.

CONCLUSIONS

- A majority of the IPA released to the environment is predicted to partition to the water compartment with lesser amounts partitioning to air and soil, depending upon the media to which IPA is directly released.

DATA QUALITY

- (2) Reliable with restrictions. Values are estimates using accepted methods.

REFERENCES

- Trent University. 1991. Fugacity-based Environmental Equilibrium Partitioning Model. Version 2.17. Environmental Modeling Centre, Trent University, Peterborough, Ontario.

OTHER

BIODEGRADATION

TEST SUBSTANCE
- Isophthalic Acid (IPA)
- Remarks: 99.9% pure

METHOD
- Method/guideline: OECD 301B and Directive 79/831/EEC Annex V
- Test Type: Modified Sturm Test (aerobic)
- GLP: Yes
- Year (study performed): 1991
- Contact time (units): 16 days
- Innoculum: sewage
- Remarks field for Test Conditions:

RESULTS
- Degradation % after time: >60% degradation within 7 days
- For each time period %: 9% up to day 2; 46% up to day 5; 64% up to day 7; 77% up to day 12.
- Breakdown products: None specified.
- Remarks field for Results:

CONCLUSIONS
- IPA is readily biodegradable under aerobic conditions, with a half-life near 5-6 days.

DATA QUALITY
- (1) Reliable without restrictions

REMARKS
- While other studies reported conclusions similar to the Battelle study the Battelle study was considered key because it was a GLP study following OECD test guidelines.

REFERENCES
- Battelle Europe. 1991. Study on the "Ready Biodegradability" (Modified Sturm Test) of Isophthalic Acid. Study No: BE-EA-128-91-01-STT-02.

OTHER
- IPA is degraded by aerobic microorganisms isolated from soil and marine sediment (Keyser et al., 1976; Aftring et al., 1981). Cultures isolated from marine sediments also degraded IPA under anaerobic conditions, although by a different metabolic pathway. After an acclimation to an activated sludge inoculum over a 24-day period, 84% of IPA was consumed in a respiratory test (Lund and Rodriguez, 1984). In another screening test, 95% of COD was removed in 5 days using an acclimated activated sludge inoculum (Pitter, 1976). In a 2-week biodegradation-screening test (MITI test) using 100 ppm IPA and an activated sludge inoculum, 77.1% of BOD was removed (Japan Chemical Industry Report, 1992). Another investigator confirmed that IPA was significantly biodegradable using the MITI test (Kitano, 1978). IPA was completely degraded in eight days using a soil inoculum (Alexander and Lustigman, 1966).

ECOTOXICITY ELEMENTS

ACUTE TOXICITY TO FISH

TEST SUBSTANCE

- Isophthalic Acid (IPA)
- Remarks: 99.9% pure

METHOD

- Method/guideline: OECD 203
- Type (test type): acute toxicity test - fish
- GLP: yes
- Year (study performed): 1991
- Species/Strain/Supplier: *Leuciscus idus melanotus*
- Analytical monitoring: High performance liquid chromatography (HPLC)
- Exposure period (unit): 96 hours
- Statistical methods: descriptive
- Details of test: static
- Remarks: Fish were exposed to test substance added to water at a range of concentrations for 96 hours. Mortalities were recorded at 24 hour intervals. The pH of the stock solution was adjusted to the required physiological value (7.8) using sodium hydroxide prior to the start of the study and was monitored daily thereafter. Adjustment of the stock solution increased the solubility of the test material. The authors believe that after pH adjustment isophthalic sodium salt was the test material investigated. The conductivity and alkalinity of the solutions were measured in addition to other parameters because addition of sodium hydroxide altered the physico-chemical properties of the test solution. A "salinity control" was added to the study to determine if the altered physico-chemical properties could cause any effect.

RESULTS

- Nominal concentrations: 130, 220, 350, 600, and 1000 mg/L
- Measured concentrations: The analytically determined actual concentrations of the test material at the beginning of the study ranged from 91 to 98% (aver age of 94.2%) of the nominal concentration. The analytically determined stability after 96 hours of exposure, were found to be within the range of 28% to 92% (average of 59%) of the nominal values.
- Element value: LC0 value exceeds 1,000 mg/L, LC50 (96 hr) could not be determined, NOEC (96 hr) > 895 mg/L based on the 96-hour average measured concentration for the highest concentration level tested.
- Statistical results:
- Remarks: The pH values during the study ranged from 7.0 to 7.8 (average 7.47).

CONCLUSIONS

- IPA has low toxicity to *Leuciscus idus melanotus*.

DATA QUALITY

- Reliability: Klimisch Code= 1.

REFERENCES

- Battelle Europe. 1993. A study of the Acute Toxicity to Fish (*Leuciscus idus melanotus*) of Isophthalic Acid.

OTHER

TOXICITY TO AQUATIC PLANTS (E.G., ALGAE)

TEST SUBSTANCE

- Isophthalic Acid (IPA)
- Remarks: 99.9% pure

METHOD

- Method/guideline: OECD 201
- Test type (static/other): static, algal growth inhibition test
- GLP: Yes
- Year (study performed): 1992
- Species/strain # and source: *Scenedesmus subspicatus* (Chodat, SAG 86.81); green alta; Supplier: Institu fur Pflanzenphysiologie.
- Element basis: Determination of cell number: THOMA Counting Chamber.
- Exposure period, date of start and end of the test [Duration]: 96 hours
- Analytical monitoring: HPTLC System
- Statistical methods: ANOVA with Bonferroni Multiple Range Test
- Remarks: The pH of the stock solution was adjusted prior to study initiation to 8.2 using sodium hydroxide. The authors believe that after pH adjustment Isophthalic Sodium Salt was the test material investigated..

RESULTS

- Nominal concentrations: 62.5, 125, 250, 500, and 1000 mg/L
- Measured concentrations: The analytically determined actual concentrations of the test material at the beginning of the study ranged from 102 – 121% (average of 110.38%) of the nominal concentration. After 96 hours of exposure, analyzed concentrations of the test material were relatively unchanged from measurements at 0 hours. Values were found to be within the range of 83% to 103% (average of 92.5%) of the nominal values.
- Unit: mg/L
- Element value: .
- NOEC, LOEC, or NOEL, LOEL: NOEC = ?1000 mg/L based on nominal concentrations; NOEC ? 969 mg/L based on the 96-hour average measured concentration of the highest concentration level tested.
- Was control response satisfactory: Yes
- Statistical results: Effects of IPA on cell growth were not statistically significant.
- Remarks: The pH of the test media range from 8.0 to 10.2 throughout the test period. The author concluded that the relatively high pH values at the end of the test (10.2 for control) were probably caused by the algal growth.

CONCLUSIONS

- Effects of IPA on algal cell growth were not statistically significant. Toxicity of IPA in algae is low.

DATA QUALITY

- Reliability: Klimisch Code= 1

REFERENCES

- Battelle Europe. 1993. A Study of the Toxicity to Algae (*Scenedesmus subspicatus*) of Isophthalic Acid. Study Number BE-EA-128-91-02-ALG-2.

OTHER

ACUTE TOXICITY TO AQUATIC INVERTEBRATES (E.G., DAPHNIA)

TEST SUBSTANCE

- Isophthalic Acid (IPA)
- Remarks: 99.9% Pure

METHOD

- Method/guideline: OECD No. 202
- Test type: Acute Immobilisation Test
- GLP: Yes
- Year (study performed): 1991
- Species/Strain: *Daphnia magna* (straus) water flea
- Test details: static
- Statistical methods: descriptive
- Exposure period: 48 hours
- Remarks: Daphnids were exposed to the test substance added to water at a range of concentrations for 48 hours. The effect measured was immobilization of the daphnids. Animals were considered to be immobile if they were not able to swim 15 seconds after gentle agitation of the test container. Immobilization was recorded at 24 and 48 hours. Four replicates, each containing 5 daphnids, were run per test substance concentration. The pH of the stock solution containing test material (1000 mg/L nominal) was 4.1 before addition of base. Enough sodium hydroxide was added to bring the final pH to 7.8. The pH of test solutions was monitored at the beginning and end of the study. Values ranged from 7.7 to 7.9. The authors believe that after pH adjustment isophthalic acid and isophthalic sodium salt were the test materials investigated.

RESULTS

- Nominal concentrations: 80, 130, 220, 350, 600, and 1000 mg/L
- Measured concentrations: The analytically determined actual concentrations of the test material at the beginning of the study ranged from 91 – 105% (average of 97.8%) of the nominal concentration. After 48 hours of exposure, analyzed concentrations of the test material were relatively unchanged from measurements at 0 hours. Values were found to be within the range of 77% to 92% (average of 84.5%) of the nominal values.

Exposure time	Nominal concentration	Average Measured concentration
0	80	74.4
0	350	340
0	1000	1022
48	80	67
48	350	286
48	1000	876

- Unit: mg/L
- EC_{50}, EL_{50}, LC_0, LL_0, at 48 hours: EC0(48 hr) = 1000 mg/L, EC50 (48 hr) = could not be determined, NOEC > = 1000 mg/L based on nominal concentrations. EC0 (48 hr) = >876 mg/L based on the 48 hour average measured concentration of the highest concentration level tested.
- Statistical results:
- Remarks:

CONCLUSIONS

- The acute toxicity of IPA to *Daphnia magna* is low.

DATA QUALITY

- Reliability: Klimisch Code= 1

REFERENCES

- Battelle Europe. 1993. A Study of the Acute Immobilisation to DAPHNIA of Isophthalic Acid.

OTHER

TOXICITY TO BACTERIA

TEST SUBSTANCE

- Isophthalic Acid (IPA)
- Remarks: 99.9% pure

METHOD

- Method/guideline: OECD 209
- Test Type: activated Sludge, Respiration Inhibition Test
- GLP: Yes
- Year (study performed): 1991
- Innoculum: Activated sludge from a sewage plant
- Remarks : Test substance and positive control were tested at different concentration in the the test solution containing 16 ml of sewage feed, 200 ml of inoculum and deionized water to give a final volume of 500 ml. IPA was tested at 0, 1, 10, 100, 500, 1000, 2000, and 4000 mg/l . Test solutions were aerated with compressed air for 3 hours. After 3 hours test solutions were poured into an oxygen bottle and oxygen consumption was measured for 10 minutes.

RESULTS.

- EC_5: 158.3 mg/l
  EC_{25}: 353.3 mg/l
  EC_{50}: 617.1 mg/l
  EC_{75}: 1077.9 mg/l
  EC_{95}: 2405.4 mg/l
- Remarks: Respiration rates were not inhibited at concentrations in the range of water solubility of the test material (130 mg/l). Bacteria were inhibited beginning at 158.3 mg/l (EC_5). This inhibition may be due to pH shift in the solution. Positive control substance (3,5-dichlorphenol) exhibited an EC50 of 11.0 mg/l.

CONCLUSIONS

- The EC50 for for IPA was 617.1 with a 95% confidence interval: 525.2 – 725 mg/l.

DATA QUALITY

- (1) Reliable without restrictions

REMARKS

REFERENCES

- Battelle Europe. 1991. Study on the "Toxicity of Isophthalic Acid towards Bacteria According to OECD-Test Guideline 209 (Activated Sludge, Respiration Inhibition Test. Study No: BE-EA-128-91-01-BHT-02.

OTHER

HEALTH ELEMENTS

ACUTE TOXICITY

TEST SUBSTANCE

- Isophthalic Acid (IPA)
- Remarks: 99.9 % pure

METHOD

- Method/guideline: Acute oral toxicty
- Type (test type): Acute oral toxicity study
- GLP: Yes
- Year (study performed): 1990
- Species/Strain: Sprague-Dawley Rats
- Sex: male/female
- No. of animals per sex per dose: 5 males and 5 females/group
- Vehicle: water (reverse osmosis-purified)
- Route of administration: oral (gavage)
- Concentrations: A 33% (W/V) aqueous suspension of the test article was administered by oral gavage at a dosing volume of 15 ml/kg of body weight.
- Remarks: Limited gross necropsy was performed on all animals.

RESULTS

- LD50 Value: > 5000 mg/kg of body weight
- Number of deaths at each dose level: 0
- Remarks: No deaths occurred during the study. Signs observed within 24 hours following test article administration included irritability, salivation, redness around the nose, discoloration around the mouth, diarrhea, wet and/or discolored inguinal fur and discolored paws. All clinical signs observed were minor in nature and mostof the rats appeared normal 48 hours following test article administration.

Observations	Incidence	
	Males	Females
Irritability	0	1
Salivation	1	0
Diarrhea	5	5
Redness around the nose	5	3
Discoloration around the mouth	3	0
Wet inguinal fur	2	0
Discolored inguinal fur	5	1
Discolored paws	2	0

CONCLUSIONS

- The acute oral toxicity of IPA is relatively low.

DATA QUALITY

- Reliability: Klimisch Code= 1

REMARK

- Multiple acute toxicity studies were available for isophthalic acid all of which indicate the IPA has a relatively low acute toxicity. This study was chosen as the key study because it is the most current oral GLP study available. The oral route was chosen over the routes because it allows for the highest potential internal dose.

REFERENCES

- IIT Research Institute. 1990. Acute Oral Toxicity Study of Isophthalic Acid in Rats. Study No. 1553.

OTHER

- Oral LD50 (albino rat) = 12,200 mg/kg (Industrial BIO-TEST Laboratories, Inc., 1958).
- Oral LD50 (rat) = 13,000 mg/kg (Industrial BIO-TEST Laboratories, Inc., 1975).
- Oral LD 50 (rat = 10,900 mg/kg (Industrial BIO-TEST Laboratories, Inc., 1975).
- Oral LD50 (rat) = 10,400 mg/kg Marhold 1986
- 4-Hour Acute inhalation LC50 > 11,400 mg/m3 (Industrial BIO-TEST Laboratories, Inc., 1958).
- Acute Dermal LD50 > 2000 mg/kg IITRI 1990
- Acute Dermal LD50 >23,000 mg/kg (Industrial BIO-TEST Laboratories, Inc., 1958).

HEALTH ELEMENTS

ACUTE TOXICITY

TEST SUBSTANCE

- Isophthalic Acid (IPA)
- Remarks: 99.9 % pure

METHOD

- Method/guideline: Primary Eye Irritation
- Type (test type): Eye irritation
- GLP: Pre GLP
- Year (study performed): 1985
- Species/Strain: New Zealand Albino rabbit
- Sex: male/female
- No. of animals per sex per dose: 3 males and 3 females
- Vehicle: none
- Concentrations: 0.1 grams of undiluted IPA
- Remarks: IPA was administered undiluted at a dose of 0.1 grams into one eye of each of six rabbits, with the other eye serving as the untreated control. The treated eye was scored for irritation at 1, 2, 3, 4, 7, and 14 days following test article administration. Irritation was scored using the Draize method. A reaction was considered positive if at any observation period, the test article produced ulceration or opacity of the cornea (cornea score > than 0), inflammation or slight circumcorneal injection of blood vessels of the iris (iris score > 0), any obvious conjunctival swelling with partial eversion of the lids (chemosis score 2 or greater), or conjunctival erythema of diffuse crimson red (erythema score 2 or greater) with individual vessels not easily discernable

RESULTS

- Slight ocular irritation was seen in all rabbits during the study, but only three rabbits exhibited positive reactions. All scores for cornea and iris were zero.

Conjunctiva scores (A=erythema, B=chemosis, C=discharge)

Sex	Day 1			Day 2			Day 3			Day 4			Day 7			Day 14		
	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
M	1	2	1	1	1	0	0	0	0	0	0	0		0	0	0	0	0
M	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M	1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
F	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
F	2	2	0	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0
F	2	1	0	1	1	0	0	1	0	0	1	0	0	0	0	0	0	0

The maximum eye irritation score of 5.3/110 was obtained 1 day after administration of test article. Complete recover was evident by the final scoring.

CONCLUSIONS

- IPA is slightly irritating to eyes.

DATA QUALITY

- Reliability: Klimisch Code= 1

REMARK

- Multiple eye irritation studies were available for isophthalic acid. This study was choosen as the key study because it is the most current, detailed study available.

REFERENCES

- IIT Research Institute. 1985. Primary Eye Irritation Study of IPA in Rabbits. Study No. 869

OTHER

ACUTE TOXICITY

TEST SUBSTANCE
- Isophthalic Acid (IPA)
- Remarks: 99.9 % pure

METHOD
- Method/guideline: Abbreviated Dermal Irritancy/Corrosivity Study
- Type (test type): skin irritation
- GLP:
- Year (study performed): 1990
- Species/Strain: New Zealand White rabbit
- Sex: male/female
- No. of animals per sex per dose: 2 males and 1 females
- Vehicle: none
- Concentrations: 0.5 grams of undiluted IPA
- Remarks: IPA was administered undiluted at a dose of 0.5 grams to the shaved backs of three rabbits. The application site was covered with an adhesive dressing. After 4 hours the dressings were removed, the application site was rinsed with 0.9% saline and dried. The skin of the animal was scored for irritation at 30-60 minutes, 24, 48, and 72 hours following removal of the wrappings. Skin reactions were graded according to the Draize method.

RESULTS
- There was no evidence of edema, erythema and or eschar formation in any of the test animals at any of the time points. The irritation score was 0.0/8.0 at all time points, the primary dermal irritation score was 0.0.

CONCLUSIONS
- IPA is not a skin irritant.

DATA QUALITY
- Reliability: Klimisch Code= 1

REMARK
- Multiply irritation studies were available for IPA all of which showed similar findings. This study was chosen as the key study because it was the most recent and follows current protocols.

REFERENCES
- IIT Research Institute. 1990. Abbreviated Acute Dermal Irritancy/Corrosivity Study of Isophthalic acid in Rabbits. Study No. 1552

OTHER

REPEATED DOSE TOXICITY

TEST SUBSTANCE

- Isophthalic Acid (IPA)
- Remark: Purity not stated in the report though purity was generally greater than 98.5% at the time of the study.

METHOD

- Method/guideline followed: Subacute feeding study
- Test type: Oral repeated-dose toxicity study
- GLP (Y/N): Pre-GLP
- Year (study performed): 1972
- Species: Rat
- Strain: Wistar-derived stock
- Route of administration: oral (diet)
- Duration of test: 13 weeks
- Doses/concentration levels: 0, 0.5, 1.6, and 5.0%
- Sex: male & female
- Exposure period: 13 weeks
- Frequency of treatment: daily
- Control group and treatment: feed
- Post exposure observation period: 0
- Statistical methods: descriptive
- Remarks field for Test Conditions. Assumes a default food intake of 0.05 kg/kg body weight-day for rats, the feed concentrations correspond to doses of 0, 250, 800, and 2500 mg IPA/kg body weight-day, respectively. Following the first week of the study the weight gains of the rats were examined. It was concluded that the 5% dose level would not permit growth. Therefore the high dose was reduced to 3% or approximately 1500 mg/kg.
- Test Subjects
  - Age at study initiation: 28 days
  - No. of animals per sex per dose: 450 rats total, 25 males and 25 females in both control groups, the remainder equally distributed across test groups.
- Study Design
  - Vehicle: feed
  - Clinical observations performed and frequency: daily
  - Organs examined at necropsy: Liver, spleen, stomach, small intestine, large intestine, pancreas, kidneys, ureters, urinary bladder, adrenals, gonads, thyroids, pituitary, thymus, salivary gland, lymph nodes, heart, lungs, bone marrow, skin, skeletal muscle, and brain.

RESULTS

- NOAEL (NOEL): 250 mg/kg-day
- LOAEL (LOEL): 800 mg/kg-day
- Toxic response/effects by dose level:

	Incidence			
Approximate Dose (mg/kg-day)	**Renal Pathology Male**	**Female**	**Crystalluria* Male**	**Female**
0	1/25	4/25	0/5	0/5
250	1/25	5/25	0/5	0/5
800	5/25	4/25	1/5	2/5
2500/1500	4/25	7/25	3/5	3/5

* Only five animals per test group were evaluated for crystalluria.

Levels of 1.6% (approximately 800 mg/kg-day) in the feed produced small increases in the incidence of crystalluria (1/5 males, 2/5 females) and renal pathology (mild hydronephrosis and pelvic calcification) 5/25 males 4/25 females.

CONCLUSIONS

- No adverse responses associated with the ingestion of IPA on total or differential leukocyte counts, total erythrocyte counts, hemoglobin, or hematocrit levels were noted. In addition, no adverse effects were noted on blood urea nitrogen, fasting blood glucose, serum glutamic pyrumic transaminase, or serum alkaline phophatase levels. Examination of organs at necropsy revealed no effect of treatment. This study identifies a NOAEL of 250 mg/kg-day and a LOAEL of 800 mg/kg-day based on a small increase in the incidence of kidney effects and crystalluria.

DATA QUALITY

- Reliability: (1) valid without restriction

REMARK

- Only one other repeat dose study was available for isophthalic acid, which was a 4-week inhalation study (IITRI 1988). Both this study and the inhalation study were considered valid though this study was considered key for the repeat dose endpoint because it was of longer duration (13 weeks versus 4 weeks). The 4-week inhalation robust summary is included under the toxicokinetics heading.

REFERENCES

- Vogin, E.E. 1972 . Subacute Feeding Studies (13-week) in Rats with Dimethylterephthalate (DMT), Isophthalic Acid (LA), and Terephthalic Acid (TA). Food and Drug Research Laboratories. Incorporated, Laboratory No.0411

GENETIC TOXICITY ELEMENTS

GENETIC TOXICITY IN VITRO (Mammalian Cell Gene Mutations)

TEST SUBSTANCE

- Isophthalic Acid (IPA) Remarks: 99.9 % pure

METHOD

- Method/guideline: CHO/HGPRT Mutation Assay with Confirmation (Machanoff, et al., 1981; O'Neill et al., 1977) (OECD 476)
- Type (test type): In vitro mammalian mutation assay
- GLP: Yes
- Year (study performed): 1991
- Cells: Chinese Hamster Ovary
- Concentration levels: Initial assay - 125 (only in non-activated study), 250, 500, 1500, 2000, 3000 ug/l. Confirmatory assay – 500, 1000, 2000, 3000, 3200, 3500, 4000 ug/ml in the absence and presence of activation
- Exposure period: 5 hours
- Statistical methods: descriptive
- Remarks: Doses were selected based on a preliminary cytotoxicity test. Cells were exposed to concentrations of test article ranging from 0.5 to 5000 ug/ml in the presence and absence of activation system. Significant cytotoxicity was noted at the 5000 ug/ml concentration as indicated by the cloning efficiency (0% and 13% in the absence and presence of activation)
- Control groups: ethyl methanesulfonate, benzo(a)pyrene, DMSO
- Criteria for evaluating results: Positive in the event of a dose-dependant increase in mutant frequencies with at least two consecutive doses showing mutant frequencies which are elevated above 40 mutants per 10^6 clonable cells.
- Criteria for determination of a valid test: Cloning efficiency of the solvent an untreated controls must be greater than 50%. The spontaneous mutant frequency in the solvent an untreated controls must fall within the range of 0-25 mutants per 10^6 clonable cells. The positive control must induce a mutant frequency at least three times that of the solvent control.

RESULTS

- Cytotoxicity:

Cytotoxicity as measured by cloning efficiency relative to solvent control

Concentration (ug/ml)	**Initial Assay**		**Concentration (ug/ml)**	**Confirmatory Assay**	
	-	+		-	+
125	95	-	**500**	108	108
250	105	123	**1000**	117	112
500	102	102	**2000**	105	99
1000	-	106	**3000**	101	98
1500	107	98	**3200**	96	95
2000	111	90	**3500**	110	111
3000	87	69	**4000**	87	89

- = without activation

+ = with activation

- With metabolic activation: negative
- Without metabolic activation: negative

- Chromosomal Aberrations
  Mutant Frequency (mutants/10^6 clonable cells)

Concentration (ug/ml)	Initial Assay		Concentration (ug/ml)	Confirmatory Assay	
	-	+		-	+
Untreated	2	3.4	**Untreated**	<0.5	<0.6
Solvent	<0.5	11.9	**Solvent**	5.8	1.6
125	1.5	--	**500**	0.5	1.5
250	6.2	7.0	**1000**	7.6	2.0
500	3.8	11.6	**2000**	8.2	4.1
1000	--	7.6	**3000**	4.3	2.1
1500	4.3	0.5	**3200**	10.3	2.6
2000	20.8	2.8	**3500**	<0.5	1.5
3000	5.7	7.7	**4000**	<1	16.1
Ethyl methansulfonate	256	-	**Ethyl methansulfonate**	189	--
Benzo(a)pyrene	--	93	**Benzo(a)pyrene**	--	165

- = without activation
+ = with activation

- With metabolic activation: negative
- Without metabolic activation: negative

CONCLUSIONS

- Under the conditions of this assay, IPA was found to be negative in the CHO/HGPRT mutation assay.

DATA QUALITY

- Reliability: Klimisch Code= 1

REFERENCES

- Microbiological Associates, Inc. 1991. CHO/HGPRT Mutation Assay with Confirmation. Laboratory Study Number T9410.332001.

OTHER

GENETIC TOXICITY IN VITRO (mammalian cell chromosomal aberrations)

TEST SUBSTANCE

- Isophthalic Acid (IPA)
- Remarks: 99.9 % pure

METHOD

- Method/guideline: Chromosomal abberation (Preston, et al., 1981; Perry and Wolff, 1974) (OECD 473)
- Type (test type): chromosomal aberration
- GLP: Yes
- Year (study performed): 1990
- Cells: Chinese Hamster Ovary
- With and without metabolic activation.
- Concentration levels: 625, 1250, 2500, 5000 ug/ml.
- Exposure period: 12 hours (non-activated study); 10 hours (activated study)
- Statistical methods: Analysis of the percent aberrant cells was performed using the Fisher's exact test. The Fisher's exact test was used to compare pairwise the percent aberrant cells of each treatment group with that of the solvent control. In the event of a positive Fisher's test at any test article dose level, the Cochran-Armitage test was used to measure dose-responsiveness.
- Remarks: Dose levels for the chromosome aberration assay were selected following a preliminary toxicity test based on the reduction in mitotic index after treatment relative to solvent control.
- Control groups: triethylenemelamine, cylcophosphamide, DMSO
- Criteria for evaluating results: The test article was considered to induce a positive response when the percentages of cells with aberrations are increased in a dose responsive manner with one or more concentrations being statistically elevated relative to the solvent control group ($p \leq 0.05$). A significant increase at the high dose only with no dose response was considered suspect. A significant increase at one dose level other than the high dose with no dose response was considered equivocal.

RESULTS

Treatment	S-9 Activation	Mitotic Index	% Cells with Aberrations
Untreated	-	4.7	2
DMSO	-	4.9	0
625	-	3.8	0
1250	-	3.2	0
2500	-	2.7	2
5000	-	4.2	1
Triethylenemelamine	-	2.4	18
Untreated	+	8.6	0
DMSO	+	8.9	2
625	+	8.7	1
1250	+	9.5	0
2500	+	8.9	0
5000	+	9.6	2
Cylcophosphamide	+	2.4	14

- Cytotoxicity:
  - With metabolic activation: negative
  - Without metabolic activation: negative
- Chromosomal Aberrations
  - With metabolic activation: negative
  - Without metabolic activation: negative

CONCLUSIONS

- Under the conditions of this assay, IPA was found to be negative in the CHO cytogenics assay.

DATA QUALITY

- Reliability: Klimisch Code= 1

REFERENCES

- Microbiological Associates, Inc. 1990. Chromosome Aberrations in Chinese Hamster Ovary (CHO) cells. Laboratory Study Number T9410.337.

OTHER

GENETIC TOXICITY IN VITRO (bacterial gene mutations)

TEST SUBSTANCE

- Isophthalic Acid (IPA)
- Remarks: 99.9 % pure

METHOD

- Method/guideline: Salmonella/Mammalian-Microsome Plate Incorporation Assay with Confirmation (Ames Assay) (Ames et al., 1975; Maron and Ames, 1983) (OECD 471)
- Type: mutagenicity assay
- System of testing: Bacterial
- GLP: Yes
- Year (study performed): 1990
- Cell line: Salmonella typhimurium TA98, TA1537, TA1538, TA100; Escherichia coli WP2uvrA
- Metabolic activation: Liver S-9
- Species: Rat
- Concentrations tested: 0, 667, 1000, 3333, 6667, 10000 ug/plate
- Statistical Methods: descriptive
- Number of replicates: 3
- Positive and negative control groups and treatment: 2-aminofluorene, sodium azide, 2-nitrofluorene, DMSO
- Criteria for evaluating results (e.g. cell evaluated per dose group): For IPA to be evaluated positive, it must cause a reproducible dose-related increase in the mean revertants per plate of at least one tester strain with a minimum of two increasing concentrations of test article. For strains TA1535, TA1537, TA1538 data sets were considered positive if an increase in the mean revertants at the peak of the dose response is equal to or greater than three times the mean vehicle control value. Data sets for strains TA98 and TA100 were judged positive if the increase in mean revertants at the peak of the dose response is equal to or greater than two times the mean vehicle control value.

RESULTS

- Genotoxic effects
  - With metabolic activation: positive (TA98 and TA1538)
  - Without metabolic activation: positive (TA1538)

	Average Revertants				
Dose ug/plate	**TA98**	**TA100**	**TA1535**	**TA1537**	**TA1538**
0 +	20 / 28	120 / 177	9 / 14	10 / 7	6 / 9
-	26 / 23	151 / 131	15 / 8	8 / 7	11 / 7
667 +	26 / 39	125 / 173	9 / 10	9 / 7	10 / 13
-	37 / 19	150 / 136	11 / 10	11 / 9	10 / 8
1000 +	24 / 31	132 / 171	11 / 11	11 / 9	14 / 10
-	32 / 21	147 / 146	10 / 13	10 / 9	12 / 6
3333 +	30 / 51	131 / 192	9 / 14	17 / 17	23 / 20
-	44 / 25	150 / 142	9 / 9	11 / 16	28 / 17
6667 +	53 / 62	139 / 226	12 / 12	23 / 28	37 / 39
-	54 / 24	159 / 163	11 / 11	15 / 26	60 / 41
10000 +	57 / 93	147 / 246	8 / 8	26 / 40	52 / 75
-	79 / 28	167 / 159	11 / 10	20 / 31	65 / 44

CONCLUSIONS

- IPA did cause reproducible positive responses with tester strains TA98 and TA1538 in the presence of microsomal enzymes and with tester strain TA1538 in the absence of microsomal enzymes.

DATA QUALITY

- Reliability – Klimish Code= 1.

REFERENCES

- Microbiological Associates, Inc. 1990. Salmonella/Mammalian-Microsome Plate Incorporation Mutagenicity Assay (Ames Test) with a Confirmatory Assay. Study Number: T9410.501014.

OTHER

GENETIC TOXICITY IN VITRO (Bacterial gene mutations)

TEST SUBSTANCE

- Isophthalic Acid (IPA)
- Remarks: >99.5 % pure

METHOD

- Method/guideline: Salmonella/Mammalian-Microsome Mutagenicity Test, OECD No. 471 (Ames Test) (Ames et al., 1973; Ames et al., 1975)
- Type: mutagenicity assay
- System of testing: Bacterial
- GLP: Yes
- Year (study performed): 1991
- Cell line: Salmonella typhimurium TA98, TA1535, TA1537, TA1538, TA100
- Metabolic activation: Liver S-9
- Species: Rat
- Concentrations tested: 0, 4, 20, 100, 500, 2500, 10,000 ug/plate
- Statistical Methods: descriptive
- Number of replicates: 3
- Positive and negative control groups and treatment: 2-aminofluorene, sodium azide, 2-nitrofluorene, 9-aminoacridine, benzo(a)pyrene
- Criteria for evaluating results: A dose dependent 2-fold increase in revertant colonies was considered positive.

RESULTS

- Genotoxic effects
  - With metabolic activation: positive - TA1537, TA1538, TA98
  - Without metabolic activation: positive – TA1537, TA1538, TA98

	Average Revertants				
Dose ug/plate	**TA1537**	**TA100**	**TA1535**	**TA1538**	**TA98**
0 +	7	92	5	15	22
-	8	122	6	11	22
4 +	7	106	7	13	20
-	11	137	12	8	24
20 +	7	107	6	14	23
-	7	124	7	14	24
100 +	9	99	6	14	20
-	7	127	8	13	23
500 +	13	120	7	23	19
-	10	118	6	15	25
2500 +	22	137	7	52	70
-	20	124	6	25	27
10000 +	48	218	8	151	151
-	57	188	10	133	79

CONCLUSIONS

- IPA gave a dose-dependant increase in the number of revertant colonies with the bacterial strains TA1537, TA1538, and TA98 in the absence and presence of activation.

DATA QUALITY

- Reliability – Klimish Code= 1.

REFERENCES

- Muller, W. 1991. Isophthalsaure. Study of the Mutagenic Potential in Strains of Salmonella Typhimurium (Ames Test); Study No. 91.0006.

OTHER

GENETIC TOXICITY IN VITRO (Bacterial gene mutations)

TEST SUBSTANCE

- Isophthalic Acid (IPA)
- Remarks: 99.9% pure

METHOD

- Method/guideline: OECD No. 471: Genetic Toxicology: Salmonella typhimurium Reverse Mutation Assay
- Type: reverse mutation assay
- System of testing: Bacterial
- GLP: Yes
- Year (study performed): 1991
- Cell line: Salmonella typhimurium TA98, TA1535, TA1537, TA1538, TA100
- Metabolic activation: Liver S-9
- Species: Rat
- Concentrations tested: 50, 150, 500, 1500, 5000 ug/plate
- Statistical Methods: descriptive
- Number of replicates: 3
- Positive and negative control groups and treatment: 2-aminofluorene, sodium azide, 2-nitrofluorene, dimethyle sulfoxide(DMSO), 9-aminoacridine, N-ethyl-N'-nitro-N-nitroguanidine
- Criteria for evaluating results (e.g. cell evaluated per dose group): If treatment with a test material produces an increase in revertant colony numbers of at least twice the concurrent solvent controls, with some evidence of a positive dose-relationship, in two separate experiments, with any bacterial strain either in the presence or absence of S-9 mix, it is considered to show evidence of mutagenic activity in this test system.

RESULTS

- Genotoxic effects
  - With metabolic activation: negative
  - Without metabolic activation: negative

CONCLUSIONS

- No evidence of mutagenic activity was seen at any dose level in either mutation test.

DATA QUALITY

- Reliability – Klimish Code= 1.

REFERENCES

- Huntingdon Research Centre. 1991. Amoco Isophthalic Acid 220: Bacterial Mutation Assay. AOM 2/91617.

OTHER

GENETIC TOXICITY IN VITRO (Mammalian Cell Gene Mutations)

TEST SUBSTANCE

- P.I.A. Purified Isophthalic Acid (IPA)\
- Remarks: 99.9 % pure

METHOD

- Method/guideline: Mouse Lymphoma Mutation Assay, OECD Guideline No. 476
- Type (test type): mutation assay
- GLP: Yes
- Year (study performed): 1994
- Cells: mouse lymphoma L5178Y cells
- Concentration levels: 7.5, 25, 75, 250, 750, and 2500 ug/ml (toxicity test); 150, 300, 450, 600, 750, 900, and 950 ug/ml (mutation assays)
- Exposure period: cells were incubated for 2 days following exposure
- Statistical methods:
- Remarks:
- Control groups: ethyl methanesulphonate and 3-methylcholanthrene (positive controls); DMSO (vehicle control)
- Criteria for evaluating results: A negative response was recorded if responses form the test substance were not higher than those of the vehicle control and the chemical had been tested to preset limits that included either a reduction of relative total growth to 20%, or precipitation of the test compound, or a maximum acceptable dose of 5 mg/ml.

RESULTS

- No indication of mutagenic activity was obtained in both assays (with and without S9 activation).

CONCLUSIONS

- The results of this study provide no conclusive evidence of mutagenic activity attributable to P.I.A. Purified Isophthalic Acid in mouse lymphoma L5178Y cells.

DATA QUALITY

- Reliability: Klimisch Code= 1

REFERENCES

- Inversk Research International Limited. 1994. P.I.A. Purified Isophthalic Acid Mouse Lymphoma Mutation Assay. IRI Project No. 755466.

OTHER

GENETIC TOXICITY IN VIVO

TEST SUBSTANCE

- In the absence of an in vivo genotoxicity study for IPA, it is believed that terephthalic acid (TPA), an isomer of IPA, may be used as a reasonable surrogate.

METHOD

- Type: Mammalian Erythrocyte Micronucleus assay (OECD 474)
- Species: Mouse
- Strain: ICR
- Sex: male and female
- Route of admin.: single intraperitoneal (ip) injection
- Exposure period: 24 and 48 hours
- Doses: 200, 400, 800 mg/kg
- Year : 2001
- GLP : Yes
- Remark: Terephthalic acid was supplied by the BP Amoco Chemicals Corporation. Purity was not noted but typically exceeds 99%. Animals were about 6-8 weeks of age at study initiation. Animals (5/sex/group) were dosed ip with vehic le (negative control), 200, 400 or 800 mg/kg TPA, or 50 mg/kg cyclophosphamide (positive control) in corn oil in a volume of 20 ml/kg body weight and were sacrificed at 24 hours. Additional animals (5/sex/group) were treated with vehicle or 800 mg/kg TPA and sacrificed at 48 hours. An additional group of 5 males and 5 females were dosed with 800 mg/kg TPA as a replacement group in case of mortality. Bone marrow samples from animals sacrificed at 24 and 48 hours were scored under oil immersion (2000 polychromatic erythrocytes (PCE) per animal) for the presence of micronuclei. The number of micronucleated normocytes per 2000 PCE was also assessed. The proportion of PCE to total erythrocytes was also recorded on a per 1000 erythrocyte basis. Statistical significance for the incidence of micronucleated polychromatic erythrocytes was determined using Kastenbaum-Bowman Tables. Criteria for a valid test: The mean incidence of micronucleated polychromatic erythrocytes must not exceed 5/1000 polychromatic erythrocytes (0.5%) in the negative control vehicle. The incidence rate in the positive control group must be significantly increased relative to the negative control ($p<0.05$, Kastenbaum-Bowman Tables).

RESULTS

- Negative. Mortality was observed in 1/15 male mice that had been treated with 800 mg/kg TPA. One mouse from the replacement group was used in place of the animal that died. Clinical signs following treatment with either dose of TPA included lethargy and piloerection. Negative and positive control animals appeared normal during the course of the study. The total number of micronuclei observed per 20000 PCE in animals treated with vehicle, 200, 400 or 800 mg/kg for 24 hours was 4, 8, 5, and 4, respectively. The incidence of micronuclei in animals treated with 800 mg/kg also did not differ from the vehicle control at 48 hours (2/20000 vs. 8/20000, respectively). There was no difference between males and females. TPA was negative in the test. The test was valid, as the incidence of micronuclei in the vehicle control was not greater than 5/1000 PCE and the number of micronucleated cells in the positive controls (382/20000) was significantly different ($p < 0.05$) from the vehicle control. Reductions (up to 9%) in the ratio of polychromatic erythrocytes to total erythrocytes were observed in some of the treated groups relative to the vehicle control, suggesting that the test article did not inhibit erythropoiesis. Greater reductions in this ratio were observed in animals treated with cyclophosphamide (25-29%).

DATA QUALITY

- Reliability: (1) valid without restriction

REFERENCES

- Bioreliance. 2001. Mammalian erythrocyte micronucleus test. Study No. AA41MJ.123.BTL for BP Amoco.

CARCINOGENICITY

TEST SUBSTANCE

- Terephthalic Acid (TPA)

METHOD

- Method/guideline followed: Two-year oral feeding study
- GLP (Y/N): Unknown
- Year study performed: 1983
- Species: Rat
- Strain: Fischer 344
- Route of Administration: Oral feed
- Duration of test: Lifetime (2 years)
- Doses/concentration levels: 0. 20, 142, 1000 mg/kg/day
- Sex: Male and Female
- Exposure period: Lifetime
- Frequency of treatment: Daily
- Control group: Yes concurrent no treatment
- Post exposure period: None

RESULTS :

- Terephthalic acid induced bladder stones were seen in 13/126 females in the high dose group. At the scheduled 6 and 12 month sacrifices, no bladder calculi were detected. At the 18 month sacrifice sand like particle or bladder calculi were only seen in two of the high dose females. There were 18/118 females with what was described as transitional cell adenomas by one pathology laboratory and epithelial hyperplasia by another. Two of these were detected in high dose females after 18 months (2/27), 15 were seen in seen in high dose females at the end of the study (15/79), and one was seen in a control female at the end of the study. None were found in the males, nor at any other dose level. It was believed that rats fed high concentrations of terephthalic acid in the diet develop bladder calculi which appear to cause chronic inflammation of the bladder epithelium, bladder hyperplasia and subsequently bladder tumours. An apparent threshold effect exists because animals exposed to lower concentrations for their lifetime do not form bladder calculi or tumors. The high dose group in this study (1000 mg/kg/day) corresponds to an approximate dietary concentration of 2.0% to 2.8% in adult Fisher rats.

CONCLUSION:

- Chronic dietary exposure to TPA resulted in an increase incidence of calculi, bladder hyperplasia, and bladder tumors at the highest dose tested (1000 mg/kg). The induction of bladder tumors is believed to be a result of injury to the bladder epithelium from the calculi formation.

DATA QUALITY

- Reliability: (1) Reliable without restrictions

REMARK

- Two carcinogenicity studies were available for TPA (the structural analog of IPA). This 1983 CIIT study was considered key because the report contained considerably more detail than did the 1974 study by Gross. However, it is important to note that both studies reported consistent results.

REFERENCE:

- CIIT (1983) Chronic Dietary Administration of Terephthalic Acid. CIIT Docket 20124

TOXICITY TO REPRODUCTION

TEST SUBSTANCE

- In the absence of a reproductive toxicity study for isophthalic acid (IPA), it is believed that a reproductive toxicity study of terephthalic acid (TPA), an isomer of IPA, is a reasonable surrogate for the effects of IPA.

METHOD

- Method/guideline followed: Reproductive toxicity study
- Test type: One generation
- GLP (Y/N): Y
- Year (study performed): 1982
- Species: Rat
- Strain: Wistar and CD
- Route of administration: oral (feed)
- Doses/concentration levels: 0, 0.03, 0.125, 0.5, 2.0, or 5% TPA in diet
- Sex: male and female
- Control group and treatment: feed
- Frequency of treatment: daily
- Duration of test: Throughout mating, gestation, lactation, and post weaning
- Premating exposure period for males: 90 days
- Premating exposure period for females: 90 days
- Statistical methods: descriptive

  Remarks: This study contrasted the toxicity of TPA in two different strains of rats. Experimental conditions were identical for both. Rats 15-17 weeks of age (n=30) were grouped housed 3/cage for the first 90 days of exposure. Body weight and feed intake were determined weekly during this time period. On Day 91, breeding pairs (n=10/sex) were housed together for 2 weeks prior to being separated. On Day 0 (delivery) the number and viability of offspring were evaluated and grossly examined. Offspring were recounted, sexed, and weighed on Day 1. These measurements were repeated at weaning on Day 21. After weaning the litters were reduced to 2/sex/dose from each of 5 litters (20 pups/dose/strain) and maintained on test diets for 30 more days (Day 51) prior to sacrifice. There were only 9 pairs of CD strain rats at the 5% diet level. Remaining animals were necropsied within a few days post weaning. At termination offspring were grossly examined and necropsied. Parental and F1 generation animals were observed 2x/day for clinical signs. Body weight gain and standard reproductive indices were assessed and statistically compared using ANOVA and Dunnett's-t-test using SAS statistical programs. Parameters evaluated consisted of: fertility index, number of offspring born per dam; number and proportion of each sex born; number (Day 0, 1, and 21) and proportion (Day 1 and 21) of each sex alive; average weight at Day 1 and 21 of all offspring and of each sex. The approximated mg/kg doses based on average feed consumption and body weight during the 90 day pre-mating period were: CD(M): 14, 59, 240, 930, 2499; CD(F): 17, 67, 282, 1107, 2783; Wistar(M): 14, 61, 249, 960, 2480; Wistar(F): 19, 78, 307, 1219, 3018.

RESULTS

- Parental Effects: Following 90 days of exposure to TPA, statistically significant decreases in food consumption were observed in CD females treated with 2% and 5%, and in both sexes of Wistars treated with 5%. Body weights were statistically decreased after 13 weeks in both sexes of CD rats on 2% and 5% TPA diets, and in males exposed to 0.03%. This effect occurred in Wistars (both sexes) only at the 5% level. There were 5 deaths (3 CD females, 1 Wistar/sex) reported during weeks 4-13 in animals given 5% TPA in the diet. During the one-generation component of the study 3 CD (1 male at 2.0%, 1/sex at 5.0%) and 4 Wistar female (2 at 5.0% and 2 at 0.03%) rats died. There was no effect of treatment on fertility index and litter size.

- Offspring Effects: There were no effects of treatment on litter size, sex ratio, or total number of offspring. While no control offspring were found dead on Day 0, 17 Wistar pups (1 at 0.03%, 2 at 0.125%, 1 at 0.5%, 12 at 2.0% (2 from one dam and 10 from another)) and 23 CD pups (1 at 0.5%, 7 at 2.0% (3 dams) and 15 at 5.0% (3 dams; with 11 from one of them)) were found dead. No statistical differences were noted in viability on Days 0, 1, or 21 in either strain. In CD rats, survivability on Day 21 was reduced in both sexes of offspring whose parents had been exposed to 5% TPA in the diet. In Wistar rats, body weights of both sexes of offspring from dams given 5.0% were reduced at Day 1. On Day 21, body weight was reduced in both strains of offspring from dams that ingested 5% TPA in the diet. Increased postnatal deaths on Day 1 and decreased survivability to Day 21 were noted in the 2% and 5% groups. At these dose levels, several large litters of pups were lost to dams suffering obvious signs of toxicity. Several of these dams did not allow the pups to nurse or attend to the litters. These pups were noted not to have milk in their stomachs and presented clinically as being very weak. These dams were consuming dietary levels of TPA known to cause reduced feed consumption, diarrhea and gastric trichobezoars (hairballs) and induce the formation of renal and bladder calculi. Unscheduled deaths during the postweaning period (Day 21-51) were confined to the 5% TPA group (18 Wistar and 16 CD) and were associated with a very high incidence of renal and bladder calculi. Renal and bladder calculi were noted in all animals exposed to 5% that were necropsied at Day 21. Day 51 necropsy findings also reported a very high incidence of renal and bladder calculi and the histological sequelae of the presence of the calculi.

	Response – CD Rats		
Percent in diet	**Viability of Offspring - # alive/litter – 21 days**	**Average weight (g), male and female combined – day 21**	**Renal and Bladder Calculi in offspring**
0	9.6	58.1	0
0.03	10.1	50.7	0
0.125	11.2	55.1	0
0.5	10.3	52.2	0
2.0	7.8	45.4	1m, 1f
5.0	5.8	25.2	5m, 9f

REMARK

- Other studies have demonstrated an increased incidence of renal and bladder calculi formation in weanling animals when compared to adults consuming the same dietary level of TPA. This apparent increase in sensitivity can be explained by the large amount of feed consumed in relation to body weight for young animals experiencing their growth spurt. Weanling animals are not more sensitive to TPA when the results are expressed on a mg/kg basis.

CONCLUSIONS

- The NOAEL for reproductive toxicity was >5% in the diet (approximately 2480-3018 mg/kg-day). Whereas, the NOAEL for parental and F1 generation toxicity was 0.5% (approximately 240-307 mg/kg-day) TPA in the diet.

DATA QUALITY

- (1) reliable without restriction

REMARK

- This study was chosen as the key study because it was the most extensive/detailed reproductive study available (90-day repeat dose one generation repro study in two strains of rat).

REFERENCES

- Gibson, J.E., 1982. A Ninety Day Study of Terephthalic -Induced Urolithiasis and Reproductive Performance in Wistar and CD Rats. Research Triangle Institute Experimental Pathology Laboratories Inc. Chemical Industry Institute of Toxicology.

OTHER

DEVELOPMENTAL TOXICITY/TERATOGENICITY

TEST SUBSTANCE

- Isophthalic Acid (IPA)
- Remarks: 99.9 % pure

METHOD

- Method/guideline: Segment II Inhalation Teratology Study
- GLP: yes
- Year (study performed): 1991
- Species: Rat
- Strain: Sprague-Dawley
- Route of administration: inhalation (particulate aerosol)
- Doses/concentration levels: 0, 1.0, 5.0, and 10.0 mg/m^3
- Sex: Female
- Number of pregnant females per dose: Control-16; 1.0–18; 5.0–18; 10.0–18.
- Exposure period: Gestation days 6-15
- Frequency of treatment: 6 hr/day, 7 days/week
- Control group and treatment: Filtered Air
- Duration of test: 10 consecutive exposures
- Statistical methods: Descriptive
- Remarks: All dams were subjected to a Cesarian section and gross necropsy. The uterine horns, fetuses and ovaries were removed intact trimmed and weighed. Ovaries were removed and the corpora letea were counted. Fetuses were individually weighed after the total number and disposition of each implant was recorded. Each fetus received a gross external morphological examination. One-half of each litter was randomly assigned to receive either a skeletal or a wet visceral examination.

RESULTS

- Clinical Observations: Salivation, hair loss and the forelimbs and red material around the nose/eyes/face were evident in all groups, with the incidence of these observations being similar in all groups. Discolored paws was more prominent in the exposure groups, however, the etiology of this is unknown, One dam in the 1mg/m^3 group exhibited signs of aborting on gestation days 11-19. This observation was not considered treatment related since it was confined to only one rat in the low dose group. All other clinical signs were sporadic in nature and of similar incidence in the exposed and control dams.
- Maternal toxicity: No statistically significant differences in mean dam body or uterus weights, litter weights, or dam body weight gains were evident between the IPA-exposed groups and the control groups.
- Developmental toxicity: Gross external, skeletal, and soft tissue examinations failed to show any significant increase in the incidence of fetal malformations or anomalies in the IPA-exposed litters compared to the controls.

Maternal Reproduction and litter viability Data

Parameter	Study Group Isophthalic Acid mg/m^3			
	Control	1	5	10
Average Litter size	11.6	11.2	13.4	10.7
Male : female ratio	0.8:1	0.9:1	0.9:1	0.9:1
Mean resorptions	1.12	1.12	0.83	1.17

- Remarks: The gravimetrically determined time-weighted average concentrations corrected for respirability, were 0, 0.98, 4.23, and 9.07 mg/m^3 for control, low medium and high dose, respectively. UV spectrophotometric corrected TWA concentrations were 0, 0.99, 4.35, and 9.14 mg/m^3,

respectively. The mass median aerodynamic diameter was 4.52, 5.02, and 5.59 microns for the low, medium and high dose, respectively. NOAEC = 10 mg/m^3; LOAEC = none identified.

CONCLUSIONS

- Inhalation exposure of pregnant rats to IPA during the major organogenesis period did not result in any significant toxic or teratogenic effects in the dam or fetus.

DATA QUALITY

- Reliability: Klimisch Code= 1

REFERENCES

- ITT Research Institute. 1991. A Segment II Inhalation Teratology Study of Isophthahlic Acid (IPA) in Rats. Study No. 1463.

OTHER

HEALTH ELEMENTS

REPEAT DOSE/TOXICOKINETICS

TEST SUBSTANCE

- Isophthalic Acid (IPA)
- Remarks: 99.9 % pure

METHOD

- Method/guideline: Subchronic Inhalation
- Type (test type): Subchronic Inhalation
- GLP: No
- Year (study performed): 1988
- Species/Strain: Sprague-Dawley Rats
- Sex: male/female
- No. of animals per sex per dose: 10 males and 10 females/group
- Exposure period: 4 weeks
- Frequency of Treatment: 6 hours/day 5 days per week
- Route of administration: Inhalation
- Dose/Concentrations: 1.0, 5.0, and 10 mg/m^3
- Control group Treatment: Filtered air
- Post exposure observation period: 3 weeks; 5 rats per sex designated for pre-exposure, single exposure, and weekly serum analysis for IPA were included in the control and high exposure groups. These animals were retained for 3 weeks after the last exposure to monitor diminishing serum levels of IPA.
- Statistical methods: Means and standard deviations were calculated for all quantitative parameters. Data were log transformed and statistically analyzed using both multivariate and univariate two-factor fixed effects analysis of variance (ANOVA). Body weights were evaluated using a multivariate repeated-measures analysis of variance to determine the shape of the dose response relationship over time.
- Remarks: Serum samples were collected immediately pre exposure, immediately after the first exposure, and weekly thereafter for the duration of the exposure (4 weekly samples). Samples were collected one week after the last exposure and were found to have returned to zero so no additional samples were collected.
- Study Design
  - Clinical Observations performed and frequency: Daily
  - Organs examined: Liver, spleen, duodenum, jejunum, ileum, cecum, colon,, pancreas, kidneys, urinary bladder, adrenals, gonads, epididymides, eyes, esophagus, thyroids, pituitary, thymus, salivary gland, lymph nodes (mandibular, respiratory, and mesenteric), mammary gland, nasal turbinates, prostate and seminal vesicles, sciatic nerve, spinal chord, sternum, stomach, tongue, trachea, uterus, ear, heart, lungs, femur and bone marrow (smear), skin, skeletal muscle, and brain.

RESULTS

- NOAEL (NOEL): 10 mg/m^3
- Remarks: The analytical time weighted average concentrations were 0, 0.96, 4.59, and 9.59 mg/m3. The average particle size was 5.04, 5.59, and 5.74 microns for the low, medium, and high group respectively. The proportion of respirable size particles (</= 10 microns) averaged 87.9% overall and 91.6%, 87.4%, 84.6% in the low medium and high exposure chambers, respectively. There were no treatment related deaths in any exposure group. Redness around the nose/eyes was increased in the exposed rats, but other minor adverse clinical signs were evenly distributed across all groups. No statistically significant differences between control and test article treated groups were detected with regard to body weight, clinical chemistry, hematology, absolute or relative organ weights or lung volumes. There were no significant difference between control and treated groups with respect to histopathology.

Blood level of IPA were detected immediately following exposure in rats exposed to 10 mg/m^3 for 6 hours/day. Levels remained elevated during the exposure period. Serum concentrations detected in female rats (5.3-9.3 ug/ml) were consistently higher than the concentrations detected in male rats (1.4-3.4 ug/ml). One week following exposure, IPA was not detected in the blood. IPA was not detected in the serum of any untreated rats.

IPA Serum Levels (ug/ml) for 10 mg/m^3 exposure group

Number of exposures	0	1	6	11	16	20	1-week post exposure
Male	0	2.9	2.9	3.4	2.7	1.4	0
Female	0	5.5	5.3	9.3	7.5	7.3	0

CONCLUSIONS

- The NOAEL for this study was 10 mg/m^3, the highest dose tested. IPA blood levels were detected immediately following the first exposure to 10 mg/m^3 and remained elevated during the exposure period. The data suggest that a steady state is achieved fairly rapidly (on the first day of exposure) and clearance is complete within one week.

DATA QUALITY

- Reliability: Klimisch Code= 1

REMARK.

REFERENCES

- IIT Research Institute. 1988. Four-Week Inhalation Toxicity Study of Isophthalic acid in Rats. Study No. 1301.

OTHER

- Food and Drug Research Laboratories. 1972. Subacute Feeding Studies (13-week) in Rats with Dimethylterephthalate (DMT), Isophthalic Acid (LA), and Terephthalic Acid (TA).

TOXICODYNAMICS

TEST SUBSTANCE

- Isophthalic Acid (IPA)/Terephthalic acid
- Remark: Purity not stated in the report though purity was generally greater than 98.5% at the time of the study.

METHOD

- Method/guideline followed: Subacute feeding study
- Test type: Oral repeated-dose toxicity study
- GLP (Y/N): Pre-GLP
- Year (study performed): 1972
- Species: Rat
- Strain: Wistar-derived stock
- Route of administration: oral (diet)
- Duration of test: 13 weeks
- Doses/concentration levels: 0, 0.5, 1.6, and 5.0% IPA, TPA 5.0%
- Sex: male & female
- Exposure period: 13 weeks
- Frequency of treatment: daily
- Control group and treatment: feed
- Post exposure observation period: 0
- Statistical methods: descriptive
- Remarks field for Test Conditions. Assumes a default food intake of 0.05 kg/kg body weight-day for rats, the feed concentrations correspond to doses of 0, 250, 800, and 2500 mg IPA/kg body weight-day, respectively. The corresponding dose for TPA was 2500 mg/kg body weight. Following the first week of the study the weight gains of the rats were examined. It was concluded that the 5% dose level would not permit growth. Therefore the high dose was reduced to 3% or approximately 1500 mg/kg. Blood and urine samples were collected from rats in each group at 7, 30, 60, and 90 days after initiation of the test feeding.
- Analytical Method: Samples were diluted in water and pH adjusted to 9.5 with NaOH. Samples were dehydrated. Samples were then trans-esterified with trimethylphosphate in pyridine, and esters were extracted with chloroform. Samples were analyzed by gas chromotoraphy and results compared to a standard curve
- Test Subjects
  - Age at study initiation: 28 days
  - No. of animals per sex per dose: 5 rats per sex per group for days 7 and 90 and 3 rats per sex per group for days 30 and 60..
  - Vehicle: feed

RESULTS

IPA and TPA blood levels (micrograms/ml)

Level	7-Day		30-Day		60-Day		90-Day	
	M	F	M	F	M	F	M	F
IPA 0.5%	-	-	8.75	7.51	26	27.1	3.4	ND
IPA 1.6%	29	37.1	16.3	25.3	9.6	24.6	17.5	21.3
IPA 5%/3%	97	114	32	30	17.9	31.2	26.3	40.8
TPA 5%/3%	75	54	13.7	14.2	3.1	trace	15.3	7.5

(Limit of detection (5.0 micrograms/ml)

24 Hour Urine excretion of IPA and TPA (mg/24 hours)

Level	7-Days		30-Days		60-Days		90-Days	
	M	F	M	F	M	F	M	F
IPA 0.5%	40	65	33	18	62	73	64	69
IPA 1.6%	114	110	178	87	162	153	103	95
IPA 5%/3%	200	347	162	50	177	243	159	198
TPA 5%/3%	100	54	57	61	73	188	209	270

(Limit of detection 2 micrograms/ml)

CONCLUSIONS

- Blood levels of IPA and TPA (determined as total mg phthalate/ml) increased in a dose dependant manner on days 7, 30, 60, and 90. IPA and TPA levels were generally highest during the first week of exposure and declined during the course of the study, suggesting either a change in feed consumption rates or some sort of adaptation resulting in increased clearance. 24-hour urinary excretion data collected on day 7, 30, 60, and 90 indicate that urinary excretion, presumably as unchanged chemical is the primary pathway by which IPA and TPA are eliminated from the body.

DATA QUALITY

- Reliability: (1) valid without restriction

REMARK

REFERENCES

- Vogin, E.E., 1972 Subacute Feeding Studies (13-week) in Rats with Dimethylterephthalate (DMT), Isophthalic Acid (LA), and Terephthalic Acid (TA). , Food and Drug Research Laboratories, Incorporated, Laboratory No. 0411.

IUCLID DATASET FOR

ISOPHTHALIC ACID (CAS RN 121-91-5)

I U C L I D

D a t a s e t

Existing Chemical	Substance ID: 121-91-5
CAS No.	121-91-5
EINECS Name	isophthalic acid
EINECS No.	204-506-4
Molecular Formula	C8H6O4

Dataset created by: EUROPEAN COMMISSION - European Chemicals Bureau

This dossier is a compilation based on data reported by the European Chemicals Industry following 'Council Regulation (EEC) No. 793/93 on the Evaluation and Control of the Risks of Existing Substances'. All (non-confidential) information from the single datasets, submitted in the IUCLID/HEDSET format by individual companies, was integrated to create this document.

The data have not undergone any evaluation by the European Commission.

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1.0.1 OECD and Company Information

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Telex: 311284

1.0.2 Location of Production Site

-

1.0.3 Identity of Recipients

-

1.1 General Substance Information

Substance type: organic
Physical status: solid

1.1.1 Spectra

-

1.2 Synonyms

1,3-benzenedicarboxylic acid
Source: DSM Resins BV Zwolle

3D CONCORD
Source: Amoco Chemical Company Gerrards Cross

A13-16107
Source: Amoco Chemical Company Gerrards Cross

acide benzenedicarboxylique 1,3
Source: Rhodia Belle Etoile SAS St Fons

Acide Isophtalique
Source: Amoco Chemical Company Gerrards Cross

Acide m Phtalique
Source: Rhodia Belle Etoile SAS St Fons

Benzene-1,3-dicarboxylic acid
Source: Amoco Chemical Company Gerrards Cross

HSB 2090
Source: Amoco Chemical Company Gerrards Cross

IPA
Source: Amoco Chemical Company Gerrards Cross

IPA, m-benzenedicarboxylic acid, m-phthalic acid, isoterephthalic acid, m-carboxybenzoic acid, m-dicarboxybenzene, 1,3 benzenedicarboxylic acid, Isophthalic acid
Source: SISAS S.p.A. MILANO

Isophthalate
Source: Amoco Chemical Company Gerrards Cross

Isophthalic acid
Source: Amoco Chemical Company Gerrards Cross

Isophthalic-acid
Source: Nordic Synthesis AB Karlskoga

Isophthalsaeure
Source: Bayer AG Leverkusen

Isoterephthalic acid
Source: Amoco Chemical Company Gerrards Cross

Kyselina Isoftalova
Source: Amoco Chemical Company Gerrards Cross

m-Benzenedicarboxylic acid
Source: Amoco Chemical Company Gerrards Cross

m-Phthalic acid
Source: Amoco Chemical Company Gerrards Cross

PIA
Source: Amoco Chemical Company Gerrards Cross

1.3 Impurities

-

1.4 Additives

-

1.5 Quantity

Quantity 100 000 - 500 000 tonnes

1.6.1 Labelling

-

1.6.2 Classification

-

1.7 Use Pattern

Type: type
Category: Non dispersive use

Type: type
Category: Use resulting in inclusion into or onto matrix

Type: industrial
Category: Chemical industry: used in synthesis

Type: industrial
Category: Polymers industry

Type: use
Category: Intermediates

1.7.1 Technology Production/Use

-

1.8 Occupational Exposure Limit Values

Type of limit: TLV (US)
Limit value: 10 mg/m3
Source: Amoco Chemical Company Gerrards Cross

1.9 Source of Exposure

-

1.10.1 Recommendations/Precautionary Measures

-

1.10.2 Emergency Measures

-

1.11 Packaging

-

1.12 Possib. of Rendering Subst. Harmless

-

1.13 Statements Concerning Waste

-

1.14.1 Water Pollution

Classified by: other: Bayer AG
Labelled by:
Class of danger: 0 (generally not water polluting)
Source: Bayer AG Leverkusen

1.14.2 Major Accident Hazards

-

1.14.3 Air Pollution

-

1.15 Additional Remarks

-

1.16 Last Literature Search

-

1.17 Reviews

-

1.18 Listings e.g. Chemical Inventories

-

2.1 Melting Point

Value: = 345 - 348 degree C
Decomposition: yes
Sublimation: yes
Method: other
GLP: no data
Source: Amoco Chemical Company Gerrards Cross

2.2 Boiling Point

Value:
Remark: Boiling point not applicable. Product sublimes.
Source: Amoco Chemical Company Gerrards Cross

2.3 Density

Type: relative density
Value: = 1.54 g/cm3 at 20 degree C
Method: other
GLP: no data
Source: Amoco Chemical Company Gerrards Cross

2.3.1 Granulometry

-

2.4 Vapour Pressure

-

2.5 Partition Coefficient

log Pow: ca. -2.38 - -2.32 at 20 degree C
Method: OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year:
GLP: yes
Remark: The octanol/water partition coefficient of Isophthalic Acid (IPA) was determined according to the OECD Guideline for Testing of Chemicals, No. 107, "Partition Coefficient (n-octanol/water)".

A small quantity of the tet article was added to a containerwith n-octanol and water. The flask was shaken for 1/2 hourand then centrifuged at 1500 rpm for 5 minutes to separate the two phases. The concentration of the test article in each phase was determined analytically using a HPLC procedure. The partition coefficient (the ratio of the octanol to water concentration) was calculated for each of three test conditions consisting of varying rations of octanol to water. Three replicates were prepared at each condition.

The mean partition coefficient determined for all three conditions was 0.00468. The mean log(Kow) was -2.34. Therewas no trend in the partition coefficient with varying amounts of water. The log (Kow) ranged from -2.32 to -2.38. Complete recovery of IPA was achieved (the mean recovery was 95.%, with a range of 92.6 to 98.1%). Therefore, under the conditions used in this study, the n-octanol/water partition coefficient of Isophthalic Acid was 0.00468, with a log(Kow) of -2.34.

Source: Amoco Chemical Company Gerrards Cross

(1)

2.6.1 Water Solubility

Value: <= .013 at 25 degree C
Qualitative: of very low solubility
pKa: 3.46 at 25 degree C
Method: other
GLP: no data
Source: Amoco Chemical Company Gerrards Cross

2.6.2 Surface Tension

-

2.7 Flash Point

-

2.8 Auto Flammability

-

2.9 Flammability

-

2.10 Explosive Properties

-

2.11 Oxidizing Properties

-

2.12 Additional Remarks

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3.1.1 Photodegradation

-

3.1.2 Stability in Water

-

3.1.3 Stability in Soil

-

3.2 Monitoring Data (Environment)

-

3.3.1 Transport between Environmental Compartments

-

3.3.2 Distribution

-

3.4 Mode of Degradation in Actual Use

-

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge, domestic
Concentration: 10 mg/l related to Test substance
Degradation: = 85.3 % after 14 day
Result: readily biodegradable
Kinetic:

2 day	= 8.5 %
5 day	= 45.7 %
7 day	= 64 %
12 day	= 76.8 %
16 day	= 85.3 %

Method: OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Isophthalic acid was tested for biodegradability according to 'modified Sturm'Test (OECD Guideline 301 B). Calculated from the organic carbon content of the test substance and the measured CO2 generation, 85.3% of the theoretical CO2 (ThCO2) has been generated by the test substance within 14 days in the case of the 10 mg test substance/L - culture. Alevel >60% was reached within 7 days in this test solution. 90.1% of the theoretical CO2 (ThCO2) has been generated by the test substance within 14 days in the case of the 20 mg test substance/L - culture. A level >60% was reached within5 days in that test solution. From these data obtained Isophthalic Acid should be regarded as "readily biodegradable".

Source: Amoco Chemical Company Gerrards Cross
(2)

Type: aerobic
Inoculum: activated sludge, domestic
Concentration: 20 mg/l related to Test substance
Degradation: = 90.1 % after 14 day
Result: readily biodegradable
Kinetic:
2 day = 28.6 %
5 day = 69.8 %
7 day = 76.4 %
12 day = 83.4 %
16 day = 90.1 %
Method: OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Isophthalic acid was tested for biodegradability according to 'modified Sturm-Test' (OECD Guideline 301B). Calculated from the organic carbon content of the test substance and the measured CO2 generation, 85.3% of the theoretical CO2 (ThCO2) has been generated by the test substance within 14 days in the case of the 10 mg test substance/L - culture. Alevel >60% was reached¿within 7 days in this test solution. 90.1% of the theoretical CO2 (ThCO2) has been generated by the test substance within 14 days in the case of the 20 mg test solution/L - culture. A level >60% was reached within 5 days in that test solution. From these data obtained Isophthalic Acid should be regarded a "readily biodegradable".
Source: Amoco Chemical Company Gerrards Cross
(3)

3.6 BOD5, COD or BOD5/COD Ratio

-

3.7 Bioaccumulation

-

3.8 Additional Remarks

-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: static
Species: Leuciscus idus melanotus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: >= 1000
LC0: > 1000
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1984 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: LC50 (96 hour) could not be determined.

In accordance with GLP regulations, the acute toxicity of Isophthalic Acid to the fish Leuciscus idus melanotus (Linne1758), Golden orfe, was investigated in a static test systemduring a test period of 96 hours. The study was performed according to the OECD Guideline 203, 1984 and according to "German Water Endagnerment Classification Scheme, DIN 38 412, Part 15", adopted 1982.

The nominal concentrations to which the test organisms were exposed were 130, 220, 350, 600, and 1000 mg/L Isophthalic acid.

The analytically determined actual concentrations of the test material int he tet solutions at the beginning of the study were found to be within the range of 91% and 98% with an average of 94.2%.

Before starting the test, the pH of the stock solution was adjusted to the required physiological value. It is believed that after pH adjustment Isophthalic Sodium Salt was the test material investigated in this test rather than Isophthalic Acid.

The analytically determined stability of the test material in the test solutions after 96 hours of exposure was found to be within the range of 28% and 92% of the nominal values with an average of 59%.

Based on the nominal concentrations the study resulted in the following values:

LC0 (96 h): >1000 mg/L Isophthalic Acid and Isophthalic Sodium Salt
LC50 (96 h): could not be determined
No Observed Effect Concentration (NOEC 96 h): >= 1000 mg/L Isophthalic Acid and Isophthalic Sodium Salt.

Based on the measured average concentration of the highest concentration level tested (nominally 1000 mg/L) the result of the study was LC0 (96 h) > 895 mg/L Isophthalic Acid andIsophthalic Sodium Salt

Source: Amoco Chemical Company Gerrards Cross

(1)

4.2 Acute Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: >= 1000
EC0: = 1000
Method: OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year: 1984 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: EC50 (48 h) could not be determined.

Based on the measured average concentrations of the highest concentration level tested (nominally 1000 mg/L), the resultof the study was ED0 (48 h) > 876 mg/L Isophthalic Acid and Isophthalic Sodium Salt.
The nominal concentrations to which the test organisms were exposed were 80, 130, 22, 350, 600 and 1000 mg/L IsophthalicAcid.

The analytically determined actual concentrations of the test material at the beginning of the study were found to bewithin the range of 91% and 105% with an average of 97.8%.

After 48 hours of exposure, analysed concentrations of the test material were relatively unchanged from measurements at0 hours. They were found to be within the range of 77% and 92% of the nominal values with an average of 84.5%.
Source: Amoco Chemical Company Gerrards Cross

(1)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus subspicatus (Algae)
Endpoint: growth rate
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: >= 1000
Method: OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year: 1984 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: The nominal concentrations to which the test organisms were exposed were 62.5, 125.0, 250.0, 500.0 and 1000.0 mg/L Isophthalic Acid.

The analytically determined actual concentrations of the test material at the beginning of the study were found to bewithin the range of 102% and 121%, with an average of 110.3%.

After 96 hours of exposure, analysed concentrations of the test material were relatively unchanged from measurements at0 hours. They were found to be within the range of 83% and 103% of the nominal values with an average of 92.5%.

Based on the measured average concentrations of the highest concentration level tested (nominally 1000 mg/L) the result of the study was: NOEC >= 969 mg/L Isophthalic Acid and Isophthalic Sodium Salt.
Source: Amoco Chemical Company Gerrards Cross

(1)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: activated sludge of a predominantly domestic sewage
Exposure period:
Unit: mg/l **Analytical monitoring:** no data
EC50: = 617.1
Method: OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: The actual test values were:
EC5 = 158.3 mg/L
EC25 = 353.3 mg/L
EC50 = 617.1 mg/L
EC75 = 1077.9 mg/L
EC95 = 2405.4 mg/L
The concentrations of test material used in the definitive test were 500, 1000, 2000, and 4000 mg/L Isophthalic Acid.
Source: Amoco Chemical Company Gerrards Cross

(2)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

-

4.5.2 Chronic Toxicity to Aquatic Invertebrates

-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

-

4.6.2 Toxicity to Terrestrial Plants

-

4.6.3 Toxicity to other Non–Mamm. Terrestrial Species

-

4.7 Biological Effects Monitoring

-

4.8 Biotransformation and Kinetics

-

4.9 Additional Remarks

-

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: = 10900 mg/kg bw
Method: other
Year: **GLP:** no
Test substance:
Source: Amoco Chemical Company Gerrards Cross

(1)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: > 5000 mg/kg bw
Method: other
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Isophthalic Acid was prepared as a 33% (w/v) aqueous suspension in reverse osmosis-purified water and administered by oral gavage to a group of five male and fivefemale Sprague-Dawley rats. The animals were administered 5grams of test article per kg of body weight, at a dosing volume of 15 mg/kg.

No deaths occured during the study. Therefore, the median acute lethal oral dose (LD50) of Isophthalic Acid was estimated to be greater than 5 g/kg of body weight.

Clinical sings observed during the study were minor in nature and most of the rats appeared normal within 48 hours follwoing test article administration; no clinical signs were evident at study termination. Mean body weights increased during the study and gross necropsy findings were within normal limits in all rats.
Source: Amoco Chemical Company Gerrards Cross

(1)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: = 10400 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: Route: oral
Species: rat
Study type: LD50
Dose: 10400 mg/kg
Effect: Details not reported
Source: Amoco Chemical Company Gerrards Cross

(4)

5.1.2 Acute Inhalation Toxicity

-

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rabbit
Sex:
Number of Animals:
Vehicle:
Value: > 2000 mg/kg bw
Method: other
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Isophthalic Acid was applied at a dose of 2 gram/kg body weight to the shaved backs of five male and five female rabbits. The test article was left in contact with the skinfor 24 hours and then removed. The rabbits were observed during this time and for 14 days thereafter.

No deaths occured during the study. Therefore, the median acute lethal dermal dose was estimated to be greater than 2000 mg/kg of body weight.

Mild dermal irritation (i.e., erythema) was observed within the application site of four rabbits immediately following unwrapping. Otherwise, no adverse treatment-related clinical signs were observed in any rabbit during the study. Mean body weights increased during the study. No gross pathological lesions attributable to treatement were evident in any of the rabbits at necropsy.
Source: Amoco Chemical Company Gerrards Cross

(1)

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 4200 mg/kg bw
Method: no data
Year: **GLP:** no data
Test substance: no data
Remark: Route: intraperitoneal
Species: mouse
Study type: LD50
Dose: 4200 mg/kg
Effect: Behavioral (Somnolence; Excitement)
Effect: Nutritional and gross metabolic (Body temprature decrease)
Source: Amoco Chemical Company Gerrards Cross

(5)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.: not irritating
Method: Draize Test
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Isophthalic acid was applied for 4 hours to the shaved backsof three rabbits at a dose of 0.5 g. Following unwrapping, the test sites were rensed with approximately 2 ml of 0.9% saline. All test sites were examined for signs of dermal irritation (i.e., edema, erythema and/or eschar formation) and corrosivity (i.e., ulceration and/or necrosis) 30-60 minutes, 24, 48, and 72 hours follwoing removal of the wrappings.

The irritation score was 0.0/8.0 at all time points follwoing unwrapping. The Primary Dermal Irritation Score for Isophthalic Acid was 0.0.

No signs of dermal irritation or corrosivity were seen in any rabbit during the study.
Source: Amoco Chemical Company Gerrards Cross

(1)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.: not irritating
Method: other
Year: **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Remark: 500 MG UNDILUTED ISOPHTHALIC ACID ADMINISTERED FOR A 24 HOUR EXPOSURE PERIOD, OCCLUDED SITES

SCORE: = 0.4/8.0
Source: Amoco Chemical Company Gerrards Cross

(1)

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: not irritating
EC classificat.: not irritating
Method: other
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Isophthalic acid was administered undiluted at a dose of 0.1 gram into one eye of each of six rabbits, with the othereye serving an an untreated control. The treated eye of each rabbit was scored for irritation at 1, 2, 3, 4, 7, and 14 days following test article administration. The control eye was used for comparison.

The maximum irritation score of 5.3/110.0 was obtained 1 dayafter administration of the test article. Ocular irritationwas seen in all rabbits during the study, but only three rabbits exhibited positive reactions. Complete recovery from all signs of ocular irritation was evident in two rabbits by the 2nd day, in five rabbits by the 4th day, and in all rabbits by the final scoring interval.
Source: Amoco Chemical Company Gerrards Cross

(1)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: not irritating
EC classificat.: not irritating
Method: other
Year: **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Remark: Form administered: Instillation (100 mg, undiluted)
Source: Amoco Chemical Company Gerrards Cross
(1)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: not irritating
EC classificat.: not irritating
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: Route: eye
Species: rabbit
Dose: 500 mg/24 hr
Effect: Mild
Source: Amoco Chemical Company Gerrards Cross
(4)

5.3 Sensitization

Type: Buehler Test
Species: rabbit
Number of Animals:
Vehicle:
Result: not sensitizing
Classification: not sensitizing
Method: other
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Isophthalic acid was applied once a week at a dose of 0.3 mlof a 30% (w/w) solution in dimethylsulfoxide (DMSO) to the shaved backs of ten male guinea pigs during an induction period of three weeks. Another group of 10 male guinea pigsserved as a vehicle control and was similarly dosed with 0.3ml of undiluted DMSO. A third group of ten sham control guinea pigs was handled in the same manner, but was not treated wtih test article or vehicle. Two weeks following application of the third induction dose, the treated and

sham control guinea pigs each received a challenge dose of 0.3 ml of the 30% test article/DMSO solution; the vehicle control guinea pigs each received a challenge dose of 0.3 mlof a 70% (w/w) aqueous DMSO solution. All guinea pigs were scored for erythema approximately 24 and 48 hours following application of the first induction dose and the challenge dose.

Positive erythema reactions (i.e., a score >= 2) were observed in only one test article-treated guinea pig, compared to no vehicle or sham control guinea pigs during the challenge phase. Thus, the primary effect of treatment (treated vs. control) and the secondary effect of time of scoring (24 hr vs. 48 hr) were not statistically significant. These findings indicate that dermal sensitization did not result from repeated dermal application of Isophthalic Acid.

Source: Amoco Chemical Company Gerrards Cross

(1)

5.4 Repeated Dose Toxicity

Species: rat **Sex:** male/female
Strain: Sprague-Dawley
Route of admin.: inhalation
Exposure period: 6 hours per day
Frequency of treatment: 5 days a week for 4 weeks
Post. obs. period: 3 weeks
Doses: 0, 0.96, 4.59, 9.59 mg/m3
Control Group: yes, concurrent vehicle
Method: other
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Isophthalic acid (IPA) was administered as a particulate aerosol by inhalation at target concentrations of 1.0, .0, and 10.0 mg/m3 to three groups of 10 male and 10 female Sprague-Dawley rats each. A fourth group, of an equal size,was exposed to filtered air only and served as a control. The rats were exposed 6 hours per day, 5 days per week for four weeks. In addition, 5 rats/sex designated for pre-exposure, single exposure and weekly serum analysis for IPA were included in the control and high exposure groups. These rats were retained for three weeks after the last exposure to monitor diminishing serum levels of IPA and to evaluate recovery from IPA-induced effects.

The analytical time weighted average concentrations were 0, 0.96, 4.59, and 9.59 mg/m3 for the filtered air control, low, medium, and high exposure groups, respectively.

All of the non-serum analysis-designated rats survived the exposure regimen. Except for a higher incidence of redness around the nose/eyes in the exposure groups compared to controls, all of the IPA-exposed rats were similar to the

control rats in appearance and behavior. No significant treatment-related findings were noted at the time of necropsy or upon microscopic examinationof the tissues.

IPA was not detected in the serum of any control rat at any time during the study, but was detected in the serum of all high exposure rats immediately follwoing the first exposure. These levels remained elevated for the duration of the exposure period. Mean male concentrations ranged from 1.44 microgram/ml to 3.39 microgram/ml; mean female IPA serum concentrations were consistently higher and ranged from 5.33microgram/ml to 9.26 microgram/ml. No IPA was detected in the serum of any rat one week following the last exposure.

There were no statistically significant effects of treatmenton any body weight or organ weight parameter in the expoed rats. There were no significant differences between exposedand control rats with regard to hematology or clinical chemistry parameters.

Source: Amoco Chemical Company Gerrards Cross

(1)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium/Mammalian-microsome plate incorporation mutagenicity assay with confirmation (Strains TA98, TA100, TA1537, tA1538)
Concentration: 0, 667, 1000, 333, 6667, 10000 microgram
Metabolic activation: with and without
Result: ambiguous
Method: other
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: The results of the Salmonella/Mammalian-Microsome Plate Incorporation Mutagenicity Assay with a Confirmatory Assay indicate that under the conditions of this study, the test article Isophthalic acid did cause reproducible positive responses with tester strains TA98 (3.0 and 3.3-fold, maximum increase) and TA 1538 (5.9 and 8.3 -fold, maximum increase) in the presence of microsomal enzymes and with tester strain TA 1538 (8.7 and 6.3-fold, maximum increase) in the absence of microsomal enzymes. In addition, non-reproducible positive responses were observed with tester strain TA 1537 (5.7-fold, maximum increase) in the presence of microsomal enzymes and with tester strains TA98 (2.9-fold, maximum increase) and TA 1537 (4.4-fold, maximum increase) in the absence of microsomal enzyme.
Source: Amoco Chemical Company Gerrards Cross

(3)

Type: Bacterial gene mutation assay
System of testing: Salmonella typhimurium (Strains TA1535, TA1537, TA1538, TA98, and TA100)
Concentration: 5000, 1500, 500, 150, 50 microgram/plate
Metabolic activation: with and without
Result: negative
Method: OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: In this in vitro assessment of the mutagenic potential of Amoco isophthalic Acid 220, histidine dependent auxotrophic mutants of Almonella typhimurium (strains TA1535, TA1537, TA1538, TA98 and TA100) were exposed to the test material, diluted in dimethyl sulphoxide, which was also used as a negative control.

Two independent mutation tests were performed, in the presence and absence of liver preparations from Aroclor 1254-induced rats.

In the preliminary dose range finding study with dose levelsof up to 5000 microgram/plate no toxicity was observed. A top dose level of 5000 microgram/plate was chosen for the subsequent mutation study. Other dose levels used in the mutation assays were: 1500, 500, 50 microgram/plate.

The concurrent positive control compounds demonstrated the sensitivity of the assay and the metabolising activity of the liver preparations.

No evidence of mutagenic activity was seen at any dose levelof Isophthalic Acid in either mutation test.

It is concluded that, whent ested at dose levels up to 5000 microgram/plate in dmethyl sulphoxide, Isophthalic Acid was not mutagenic in this bacterial test system.
Source: Amoco Chemical Company Gerrards Cross

(6)

Type: Cytogenetic assay
System of testing: Chinese hamster ovary cells
Concentration: 625, 1250, 2500, and 5000 microgram/ml
Metabolic activation: with and without
Result: negative
Method: other
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: The test article, Isophthalic acid, was tested in the chromosome aberration assay using Chinese hamster ovary cells. The assay was conducted both in the absence and presence of an Aroclor-induced S-9 activation system at

doselevels of 625, 1250, 2500 and 5000 ug/ml. Metaphase cells were collected for microscopic evaluation at 12 hours after treatment in the non-activated study and 10 hours after treatment in the S-9 activated study. No increase in chromosome aberrations was observed in either the non-activated or S-9 activated test system. Isophthalic acid was concluded to be negative in the CHO cytogenetics assay.

Source: Amoco Chemical Company Gerrards Cross

(7)

5.6 Genetic Toxicity 'in Vivo'

-

5.7 Carcinogenicity

-

5.8 Toxicity to Reproduction

-

5.9 Developmental Toxicity/Teratogenicity

Species: rat **Sex:** male
Strain: Sprague-Dawley
Route of admin.: inhalation
Exposure period: 6 hours per day
Frequency of treatment: 7 days per week on gestation days 6 through 15
Duration of test: 10 consecutive exposures
Doses: 0, 1.0, 5.0, and 10.0 mg/m3
Control Group: yes, concurrent vehicle
Method:
Year: **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Isophthalic Acid (IPA) was administered as a particulate aerosol by inhalation at target concentrations of 0, 1.0, 5.0, and 10.0 mg/m3 to four groups of 16-18 timed-pregnant primiparous Sprague-Dawley rats. The rats were exposed 6 hours per day, 7 days per week on gestation days 6 through 15, for a total of 10 consecutive exposures.

The gravimetrically determined time-weighted average (TWA) concentrations, corrected for respirability, were 0, 0.98, 4.23 and 9.07 mg/m3 for filtered air control, low, medium, and high exposure groups, respectively. UV spectrophotometric corrected TWA concentrations were 0, 0.99. 4.35 and 9.14 mg/m3, respectively.

No deaths occured during the study. The incidences of clinical signs observed in the IPA-exposed rats were similarto controls. No statistically significant differences in mean dam body or uterus weights, litter weights or dam body weight gains were evident between the

IPA-exposed and filtered air control rats at any time during the study. No statistically signficant difference in pup viability was detected in the IPA-exposed rats compared to the filtered air controls. Gross external, skeletal and soft tissue examinations failed to show any significant increase in the incidence of fetal nalformations or anomalies in the IPA-exposed litters compared to the controls.

Accordingly, inhalation exposure of pregnant rats to 0.98, 4.23 or 9.07 mg/m3 of IPA during the major organogenesis period did not result in any significant toxic or teratogenic effects in the dam or fetus.

Source: Amoco Chemical Company Gerrards Cross

(8)

5.10 Other Relevant Information

-

5.11 Experience with Human Exposure

-

(1) Unpublished report.

(2) Unpublished report

(3) UNPUBLISHED REPORT

(4) Prehled Prumyslove Toxikol Org Latky 1986, pg 317, 1986

(5) C R Hebd Seances Acad Aci, vol 246, pg 851, 1958

(6) unpublished report

(7) unpublished report.

(8) unpublished reports

7.1 Risk Assessment

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SECTION 3.

TEREPHTHALIC ACID (CAS RN 100-21-0)

OECD SIDS SUBMISSIONS (SIAP AND SIAR DOSSIER) FOR TEREPHTHALIC ACID (CAS RN 100-21-0)

FOREWORD INTRODUCTION

Terephthalic Acid (TPA)

CAS N°:100-21-0

SIDS Initial Assessment Report

For

12th SIAM

(Paris, France June 2001)

Chemical Name: **Terephthalic Acid (TPA)**

CAS No.: **100-21-0**

Sponsor Country: **US (+IT)**

National SIDS Contact Point in Sponsor Country: US EPA
Dr. Oscar Hernandez
Ariel Rios Building
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460
U.S.A.

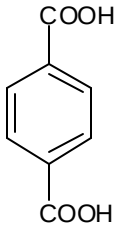
HISTORY: SIAM 3 Agenda item but not discussed in detail. Member countries requested to comment for re-draft for future SIAM.

COMMENTS:

Deadline for circulation:

Date of circulation: 20/4/2001

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	100-21-0
Chemical Name	Terephthalic acid
Structural Formula	

RECOMMENDATIONS

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Results from repeated dose and acute toxicity studies via the oral, dermal and inhalation routes indicate that terephthalic acid is of low order of toxicity, and it is non-irritating to the skin and eyes. A 15 week oral repeat dose study in rats reported a LOAEL of 3837 mg/kg b.w./day for male rates and 4523 mg/kg/day for female rats. The NOAEL is 1220 mg/kg b.w./day for male rats and 1456 mg/kg b.w./day for female rats. Repeated exposure inhalation studies up to 10 mg/m^3 (6 hours/day, 5 days/week) using rats or guinea pigs showed no adverse effects, except for mild respiratory irritation in one study with rats.

The primary adverse effect of high doses of terephthalic acid to rats is almost completely restricted to the urinary tract. These effects include formation of bladder calculi, and inflammatory changes and hyperplasia of the bladder epithelium. These urinary changes did not occur when exposure was by inhalation. Rats fed terephthalic acid (greater than 2%) 1000 mg/kg b.w./day for two years developed bladder calculi, bladder hyperplasia, and bladder tumors.

It is believed that the calculi injure the bladder epithelium and induce cell proliferation, which is probably a critical factor in the induction of bladder tumors by terephthalic acid. Bladder calculi cannot occur unless the solubility of the stone components is exceeded (i.e., unless the product of the concentrations of Ca^{++} and terephthalate in urine exceeds the solubility product of the calcium-terephthalate complex). Based on urinary solubility of Ca-terephthalate, normal human urine would become saturated with Ca-terephthalate at a terephthalic acid concentration of approximately 8 to 16 mM. Assuming that the average volume of urine excreted by humans is 1.5 liters/day, the amount of terephthalic acid that would have to be absorbed to produce the minimum saturating concentration of terephthalic acid is 2400 mg/day. It is unlikely that humans would ingest enough TPA to induce bladder calculi, and this therefore is of little concern to human health.

Terephthalic acid is not a reproductive toxicant; however, in a one-generation reproduction feeding study, postnatal developmental effects were observed in rats (LOAEL and NOAEL approximately equivalent to 1120 mg/kg b.w./day and 280 mg/kg b.w./day respectively). The adverse effects observed in the offspring appear to be the result of maternal toxicity and the formation of renal and bladder calculi in the weanling animals. No developmental effects were seen in rats when the exposure was by inhalation (NOAEC 10 mg/m^3, the highest dose tested). Terephthalic acid is not genotoxic. Terephthalic acid did not induce an increase in micronucleated polychromatic erythrocytes (micronuclei) in male or female mice *in vivo*.

Environment

Terephthalic acid (TPA) is non-toxic to aquatic organisms at concentrations lower than its water solubility (15 mg/l at 10°C). Tests were performed with a more soluble sodium salt. The values for fish acute toxicity ranged from a 96-hour LC_0 of greater than 500 mg/l to a 96-hour LC_{50} ranging from 798 to 1640 mg/l. The EC_{50} for *Daphnia* was greater than 982 mg/l and the 96-hour NOEC for *Scenedesmus subspicicatus* was greater than 1000 mg/l. Using the lowest reported LC_{50} value of the three base set tests, a PNEC value of 8 mg/l is calculated. TPA is not expected to bioaccumulate. It is subject to hydroxy radical oxidation in the atmosphere, and biodegrades in soil and surface water under aerobic conditions. Detection of terephthalic acid in air and water samples has been in the low ppt range.

Exposure

Terephthalic acid is an industrial chemical intermediate, and occupational exposures are low. In 1993, the worldwide production was estimated to be 17 to 21 million tonnes. Manufacture of polyester fibers and films accounts for a majority of TPA use. End products of polyester fiber may include yarns for carpet, apparel, fill fibers for consumer products, and industrial filaments. PET containers, the next major use, are used for a wide variety of food and beverage packaging and in other food contact uses.

NATURE OF FURTHER WORK RECOMMENDED

No further work is recommended.

SIDS FULL SUMMARY

STUDY (CAS NO.: 100-21-0)		SPECIES	PROTOCOL	RESULTS
PHYSICAL CHEMISTRY				
2.1	Melting point			> 300^0 C 402^0 C 425^0 C
2.3	Density			1.12 g/cm^3 1.50 g/cm^3 1.51 g/cm^3
2.4	Vapor pressure		Calculated (MPBPWIN)	3x10^{-11}hPa at 20^0 C 3x10^{-10} hPa at 20^{o}C 1.19 x 10^{-5}mmHg at 25^{o}C 1.33 hPa at 78^{0}C 13 hPa at 304^0 C
2.5	Partition Coefficient.		Measured	Log Kow = 1.16 to 2.00
2.6	Water solubility		Measured	15 mg/l at 10^0 C 19 mg/l at 25^{o}C
2.7	pH			
2.8	PKa			3.52 (pKa1) 4.46 (pKa2)

STUDY (CAS NO.: 100-21-0)		SPECIES	PROTOCOL	RESULTS
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		Estimate AOPWIN	Half-life: 8.6 days
3.2	Monitoring data			Detected in air at 11.1 ng/m^3. Detected in water at 3.4 µg/l (max.) Detected in sewage plant drainage at 5.3 to 13 µg/l
3.3	Environ. fate & distribution		estimate	K_{oc} = 1.855
3.5	Biodegradation			
			Modified Sturm	85.2% (10 mg/l) after 16 days 82.6% (20 mg/l) after 16 days
			Modified Sturm (performed with adapted sludge)	72% after 28 days 91% after 28 days >60% after 10 days
			Sturm	72% and 91%
			Closed Bottle	112% after 30 days 100% after 2 days
			Modified Zahn-Wellens (performed with adapted sludge)	98% after 6 days 93% after 4 days
			Zahn-Wellens	93% after 4 days
			Modified OECD screening	82% after 19 days
			Japanese MITI	30-100% after 14 days
			Aerobic Sewage Treated Coupled	93% after 1 day
3.6	COD			96% after 0.6 days 95% after 2 days
3.7	Bioaccumulation		estimate	log BCF = 3.2

STUDY (CAS NO.: 100-21-0)		SPECIES	PROTOCOL	RESULTS
ECOTOXICOLOGICAL DATA				
4.1	Acute fish	Salmo gairdneri Brachydanio rerio Leuciscus idus	OECD 203 OECD 203 OECD 203	96 hour LC_{50} = 798-1640 mg/l 96 hour LC_0 = >500 mg/l 96 hour LC_0 = >922 mg/l
4.2	Acute daphnid	Daphnia	OECD 202	48 hour EC_{50} = >982 mg/l
4.4	Acute plant	Scenedesmus subspicicatus	OECD 201	96 hour NOEC = >1000 mg/l
4.5	Bacteria, etc.	activated sludge Fasciola hepatica Tetrahymena pyriformis Caenorhabditis Elegans	OECD 209	16 day EC_{50} = 1392.8 mg/l 2 hour EC_0 = 830 mg/l 24 hour EC_{50} = 800 mg/l EC_0 = 1 µg/ml
4.6.2	Terrestrial plants	Avena sativa Oryza sativa		24 hour EC_0 = 100 mg/l 5 day EC_{20} = 100 mg/l
4.6.3	Non-mammalian species	Drosophila melanogaster		3 day LC_0 = 166 mg/kg

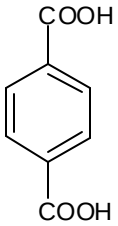
STUDY (CAS NO.: 100-21-0)		SPECIES	PROTOCOL	RESULTS
TOXICOLOGICAL DATA				
5.1	Acute Toxicity			
5.1.1	Acute oral	Rat Mouse		LD_{50} = >5000 mg/kg LD_{50} = >15380 mg/kg LD_{50} = 1960 mg/kg LD_{50} = 18800 mg/kg LD_{50} = 2000 mg/kg LD_{50} = >5000 mg/kg LD_{50} = 6400 mg/kg LD_{50} = 1470 mg/kg
5.1.2	Acute inhalation	Rat		LC_{50} = >2.02 mg/l LC_{50} = >1000 mg/m^3
5.1.3	Acute dermal	Rabbit		LD_{50} = >2000 mg/kg
5.1.4	Acute other routes	Rat Mouse Mouse		intraperitoneal LD_{50} = 1210 - 2250 mg/kg intraperitoneal LD_{50} = 880 - 1900 mg/kg intravenous LD_{50} = 770 mg/kg
5.2.1	Skin irritation	Rabbit		Non-irritating
5.2.2	Eye irritation	Rabbit		Virtually non-irritating
5.3	Skin Sensitization	Guinea pig		Not sensitizing
5.4	Repeated dose	Rat Rat Rat/guinea pig	15-week	Primary effects noted in feeding studies included bladder calculi formation and hyperplasia of the bladder epithelium. The NOAEL is 1220 mg/kg/day for male rats and 1456 mg/kg/day for female rats No adverse effects other than minimal respiratory tract irritation at inhalation exposures of 3 mg/m^3 for 4 wk. No adverse effects at inhalation exposures up to 10 mg/m^3 for 6 months.

STUDY (CAS NO.: 100-21-0)		SPECIES	PROTOCOL	RESULTS
5.5	Genetic Toxicity			
	Bacterial	Salmonella typhimurium		Not mutagenic with and without metabolic activation
	Non-bacterial	human lymphocytes Chinese hamster lung fibroblasts rat hepatocytes		No cytogenetic effects or micronuclei observed. Inactive No DNA single strand breaks
5.6	Genetic toxicity *in vivo*	Mouse	OECD 474	No increase in micronuclei in male or female mice 24 or 48 hours following i.p. injection of 200, 400 or 800 mg/kg.
5.7	Carcinogenicity	Rat	2-year	Feeding studies: Increased incidence of bladder calculi, bladder hyperplasia, and bladder tumors.
5.8	Reproductive Toxicity	Rat		No effects on fertility in one-generation feeding study up to 5% (approximately 2480–3018 mg/kg/day). Developmental effects at 2% and 5% which included postnatal deaths, decreased survivability, high incidence of renal and bladder calculi and histopathological sequelae associated with presence of the calculi. NOEL for developmental effects was 0.5% (approximately 240-307 mg/kg/day).
5.9	Teratogenicity/ Developmental Toxicity	Rat		No maternal or developmental toxicity at inhalation exposures up to 10 mg/m^3, days 6-15 of pregnancy.
5.10	Toxicokinetics			Rapidly distributed and excreted unchanged in the urine following oral or i.v. administration ($t_{1/2}$ is approx. 60-100 min). Does not readily cross the placental barrier. Neonatal rats do not develop calculi as result of ingestion of dietary terephthalic acid by their dams. Only after neonatal rats begin to self-feed from the same diet as their dams do calculi appear in the bladder of the weanling animals. Induction of calculi in urinary tract is a result of supersaturation with respect to calcium ions and terephthalic acid. Formation of calcium terephthalate.
5.11	Experience with human exposure	human		No irritation when oily paste containing 80% terephthalic acid was applied to skin for 24 hours.

SIDS INITIAL ASSESSMENT REPORT (SIAR)

1.0 IDENTITY

Chemical name: Terephthalic acid

Synonym:	1,4-Benzenedicarboxylic acid p-Phthalic acid
CAS-Number:	100-21-0
Empirical Formula:	$C_8H_6O_4$
Structural Formula:	
Physical description:	Solid white powder (it is often stored and handled in molten form).
Molecular Weight:	166
Degree of purity:	>99.9%
Melting Point	425° C
Boiling Point	Sublimes
Major impurities:	None
Essential additives:	None
Water solubility:	15 mg/L (10° C) (measured)
Partition Coefficient:	logP = 2.0 (measured)
Vapor pressure:	1.19×10^{-5} mm Hg at 25° C (calculated)
Biodegradation:	Readily biodegradable

2. 0 General Information on Exposure

2.1 General Discussion

2.1.1 Production Volume

In 1993, the U.S. production volume was estimated to be between 3.8 and 4.8 billion kg. The U.S. accounts for approximately 22% of world terephthalic acid production. In 1993, the worldwide production was estimated to be 17 to 21 billion kg.

2.1.2 Manufacturing Process

Terephthalic acid is typically produced by liquid-phase air oxidation of p-xylene in the presence of manganese and cobalt acetate catalysts and a sodium bromide promoter to form crude terephthalic acid. Crystalline crude terephthalic acid is collected as wet cake and dried. It is purified by dissolving in hot water under pressure and selectively hydrogenating contaminants catalytically. Terephthalic acid is a solid; however, it is often stored and handled in molten form.

2.1.3 Use

General: Terephthalic acid is primarily used in the manufacture and production of polyester fibers, films, polyethylene terephthalate solid-state resins and polyethylene terephthalate engineering resins.

Use in Consumer Products: Manufacture of polyester fibers accounts for a majority of terephthalic acid use. End products of polyester fiber may include yarns for carpet, apparel, fill fibers for consumer products, and industrial filaments. Polyethylene terephthalate solid-state resins are the next most common use and are used primarily for food and beverage containers. Remaining uses include polyester films, such as photographic films and magnetic tape base, and polyethylene terephthalate and polybutlyene terephthalate engineering resins used primarily in automobile parts.

2.1.4 Forms of marketed products to industrial users

Terephthalic acid is a solid white powder; however, it is often stored and handled in molten form.

2.2 Sources of potential release to the environment

2.2.1 General

Terephthalic acid is processed into polyethylene terephthalate (PET) fibers or resins at approximately 71 facilities within the United States. Releases from processing operations were estimated to be 1.1 million kg/year, with approximately 2% released to air, 1% released to land, 3% released to water, and 94% released to recycling and other offsite managements. Data on releases of terephthalic acid to the environment in the United States are limited since terephthalic acid is not required to be reported to the U.S. Environmental Protection Agency under the Toxic Release Inventory.
In 1990, terephthalic acid was de-listed from the TRI because the EPA concluded that terephthalic acid did not meet the listing criteria under section 313(d)(2) of the Emergency Planning and Community Right-to-Know Act (EPCRA), for acute human health effects, chronic health effects or chronic toxicity:

While EPA considered data which were suggestive of developmental and systemic toxicity, these data were inadequate to support a conclusion that TA can be reasonably anticipated to cause these effects in humans. It is EPA's determination that the available data do not demonstrate that TA can

cause or reasonably be anticipated to cause significant adverse human health or environmental effects. (Federal Register, Vol. 55, No. 237, December 10, 1990).

Releases of terephthalic acid to the environment from consumer uses are likely to be low because the primary use is in the manufacture of PET fibers and resins, and terephthalic acid is not marketed directly to consumers. Terephthalic acid would only be present in trace amounts in consumer end use products. Furthermore, these consumer end use products are relatively stable and do not break down in the environment to release terephthalic acid.

2.2.2 Air Releases

The primary sources for release during manufacture as a solid or melt is permitted stack air emissions, followed by fugitive air emissions. Some terephthalic acid may be found in soil due to deposition from the air releases. A draft study sponsored by the United States Environmental Protection Agency in 1994 estimated total emissions for six manufacturing sites within the United States to be approximately 196 metric tons per year for stack emissions, and 11 metric tons per year for fugitive emissions. The EPA estimates of the general population exposures potentially resulting from manufacturing releases to air within the U.S. ranged from 0.1 to <330 mg/person/year. Estimates of general population exposures potentially resulting from processing releases to air ranged from less than 1 mg/person/year to 189 mg/person/year. Although fugitive emissions of TPA have not been determined, such emissions are expected to be low, because its manufacture, use and storage take place within closed continuous equipment and it has very limited volatility. *(USEPA, Preliminary Exposure Profile: Terephthalic Acid (Draft Report), 1994)* In Japan, the atmospheric concentration was reported to be 11.1 ng/m^3 (0.0016 ppb).

2.2.3 Surface Water Releases

The maximum concentration of terephthalic acid in river water in Japan was 3.4 µg/l. *(Matsumoto, Water Res. 16, 1982)* Terephthalic acid was found in 6 out of 10 sea water samples with an average concentration of 0.7 µg/l. The samples were taken between 1974 and 1976 from an industrial coastal area. *(Kubota, Ecotoxicol. Environ. Safety 3, 256-268, 1979)*

2.3 Human Exposure

2.3.1 Consumer Exposure

Terephthalic acid is used primarily to make polyethylene terephthalate (PET) resins and fibers. The majority of end uses for PET are consumer applications. PET containers are used for a wide variety of food and beverage packaging. Terephthalic acid is non-volatile, so the potential for residual terephthalic acid off-gassing is limited. Possible consumer exposures to terephthalic acid may occur through dermal contact with PET products, as a result of consumption of food products stored in PET containers, or through the inadvertent ingestion of PET particles or films. Although there is little information in the public domain concerning residual terephthalic acid in PET, the residual level is believed to be very low. This is because the nature of the equilibrium condensation polymerization that is used to make PET requires that residual monomer levels be very low in order to produce a high molecular weight polymer such as those used in typical fiber and packaging applications. Theoretical calculations for a typical PET polymer predict that the residual terephthalic acid should be less than 10 ppm *(Eastman technical report 78-1026-650).* Migration of terephthalic acid into food simulants has been found to be less than 0.2 mg/kg food simulant even under severe test conditions (3% acetic acid, 2 hours at 100°C and HB307 synthetic triglyceride oil, 2 hours at 100°C; *Eastman technical reports 93-2866-080 and 93-2912-890*). Migration under more typical, less severe conditions of use is expected to be significantly less. Based on this information, there is very little potential for exposure to terephthalic acid from consumption of food stored in PET containers or through dermal contact.

2.3.2 Occupational Exposure

Terephthalic acid is manufactured as a solid or a melt by a small number of large producers using continuous enclosed processes, with limited occupational exposure.
Occupational exposures have been monitored on a limited basis at six U.S. manufacturing sites. Based on these monitoring data, workers in terephthalic acid loading and chemical operations are estimated to have potential inhalation dose rates ranging from <0.07 to 180 mg/day. In one U.S. manufacturing site, the air concentrations of terephthalic acid for worker exposures were an average of 1.18 mg/m^3 (range: 0.006 to 13.59 mg/m^3). These exposures do not take into account the use of respiratory protection. If respirators are used, as noted, and appropriately selected, used and maintained in accordance with an acceptable respiratory protection program, dose rates would be less than 30 mg/day. *(USEPA, Preliminary Exposure Profile: Terephthalic Acid (Draft Report), 1994)*

2.4 Environmental Exposure and Fate

2.4.1 General

Photodegradation
Terephthalic acid is expected to undergo atmospheric oxidation in air with half-life of 8.6 days. *(Syracuse Research Corporation, 1988)*

Distribution
Using default release estimates based on fugacity-based fate and transport models (Level III, *Syracuse Research Corporation, Syracuse New York*) suggest that a majority of the terephthalic acid released to the environment will partition primarily to soil (67.3%) and water (32.7%) with negligible amounts found in air (<1%) and sediment (<1%) compartments. Terephthalic acid is expected to partition to water and soil, where it will biodegrade and not persist or bioaccumulate. The pKa values of 3.52 and 4.46 indicate that TPA is nearly completely disassociated under environmental conditions. *(Bemis, Dindorf Harwood, Samans, Kirk-Othemer Encyclopedia of Chemical Technology, 3rd Ed Vol 17, 734, 1982)*

Biodegradation
Terephthalic acid is a solid with limited vapor pressure (1.33 hPa at 78°C) and low water solubility (15 mg/L at 10° C). *(Syracuse Research Corporation, 1988; ICI Chemicals and Polymer Limited, Product Safety Data, 1991)* It biodegrades readily. Using a wide variety of methods and terephthalic acid concentrations, studies report greater than 60% biodegradation under aerobic conditions. The aerobic biodegradation half-life ranged from less than a day to couple of weeks depending on the methods used. Only one studied could be found looking at anaerobic degradation. While the report concluded that the terephthalic acid degraded rapidly it did not provide sufficient detail to determine approximate anaerobic biodegradation half-life.

2.4.2 Predicted Environmental Concentrations

Modeling has been done to predict environmental concentrations of terephthalic acid arising from its manufacture and use in the United States. Estimates of environmental concentrations of terephthalic acid resulting from releases to air from manufacturing at six different facilities ranged from 1.1 ug/m^3 to 38 ug/m^3 for fugitive emissions and from 0.01 to 0.19 ug/m^3 for stack emissions. Estimates of environmental concentrations resulting from processing of terephthalic acid for fugitive and stack emissions ranged from 0.049 to 22 ug/m^3 and from 0.03 to 0.00003 ug/m^3, respectively. The model for estimating air concentrations for fugitive emissions assumes the receptor is located 100 meters downwind from the source with a release height of 3 meters. The model for estimating concentrations resulting from stack emissions assumes a receptor is located 1000 meters downwind, with a stack height of 30 meters.

Estimates of environmental concentrations in water from manufacturing discharges range from 1.8 to 168 ppb. Estimates of environmental concentrations from processing discharges range from 0.02 to 338 ppb.

Modeling results from an EPA sponsored study estimate releases to water from manufacturing may potentially expose individuals to a maximum of 103 mg/year through ingestion of drinking water. The same studies estimated that releases to water from processing terephthalic acid have the potential to expose individuals to a maximum of 48 mg/year.

3.0 HAZARDS TO THE ENVIRONMENT

3.1 Aquatic Effects

Acute toxicity

Terephthalic acid has been tested for acute toxicity in several fish species. The 96-hour LC_0 for the Golden orfe was greater than 1000 mg/l nominal (922–999 mg/l measured). *(Amoco Corporation, A Study of the Acute Toxicity to Fish (Leuciscus idus melanotus) of Terephthalic Acid. Conducted by Battelle Europe; Study # BE-EA-128-91-01-F3A-3, 1993)* The 96-hour LC_{50} for other fish species ranged from greater than 500 to 1640 mg/l depending on species. The EC_{50} (immobilzation) for Daphnia was greater than 1000 mg/l nominal (982 mg/l measured). *(Amoco Chemicals Co. (1993) A Study of the Acute Immobilisation to Daphnia of Terephthalic Acid. Conducted by Battelle Europe; Study # BE-EA-128-91-02-DAK-3, 1993*) The 96-hour NOEC for Scenedesmus subspicicatus growth was greater than 1000 mg/l (nominal). *(Amoco Corporation, A Study of the Toxicity to Algae (Scenedesmus subspicatus) of Terephthalic Acid. Conducted by Battelle Europe; Study # BE-EA-128-91-02-ALG-3, 1993).* The pH of the test solutions in the aquatic studies described above were adjusted with sodium hydroxide. Therefore, under test conditions most of the terephthalic acid was converted to the more water-soluble sodium salt. This explains why the reported LC, EC and NOEC values were above water solubility limits for the acid form.

Aquatic Toxicity Data

Test	Species	Technique	LC_0 or EC_0 (mg/l) nominal/measured	LC_{50} or EC_{50} (mg/l) nominal/measured
Acute Fish	Leuciscus idus melanotus	OECD203 (static)	1000/922-999	> 1000/>922
Acute Fish	Salmo gairdneri	OECD 203 (semistatic)	500/--	798-1640/--
Acute Fish	Brachydanio rerio	OECD 203 (static)	500/--	>500/--
Acute Immobilization	Daphnia magna	OECD 202 (static)	600/--	>1000/>982
Algal growth Inhibition	Scenedesmus subspicatus	OECD 201 (static)	>1000/927	>1000/>927

Chronic toxicity

Not available

3.2 Terrestrial Effects

Not available

3.3 Other Environmental Effects:

A theoretical log BCF of 3.2 was calculated, indicating that terephthalic acid does not bioaccumulate.

4.0 HUMAN HEALTH HAZARDS (Mammalian Toxicity)

4.1 Toxicokinetics

Terephthalic acid is absorbed from the gastrointestinal tract and is excreted in the urine apparently unchanged. (*Hoshi A. Kuretani K. (1967) Metabolism of Terephthalic acid III. Absorption of terephthalic acid from the gastrointestinal tract and detection of its metabolites. Chem Pharm Bull 15, 1979-1984*) Dermal or ocular absorption is negligible. (*Hoshi A., Yanai R., Kuretani K. (1968) Toxicity of terephthalic acid. Chem Pharm Bull 16 1655-1660*) [^{14}C]Terephthalic acid has a short elimination half-life (approximately 60-100 minutes) in the plasma; however, the apparent half-life was longer following administration by gavage. The bioavailability of terephthalic acid from oral administration is relatively low with 36% to 84% (depending on the dose) unabsorbed and eliminated in the feces. [^{14}C]Terephthalic acid does not readily cross the placental barrier. Calculi were formed in the bladders of weanling animals only after the neonatal rats began to self-feed from the same diet as their dams. Induction of calculi in the urinary tract is a result of supersaturation with respect to calcium ions and terephthalate, forming a calcium-terephthalate complex. (*Wolkowski-Tyl R., Chin T.Y., Heck Hd'A (1982) Chemical urolithiasis. 3. Pharmacokinetics and transplacental transport of terephthalic acid in Fischer-344 rats. Drug Metab Dispos 10, 486-490*)

4.2 Acute Toxicity

4.2.1 Oral

The oral LD_{50} in rats is greater than 5 g/kg, with some rats exhibiting clinical signs of diarrhea, redness around nose and discolored inguinal fur. (*Amoco Corporation, Acute Oral Toxicity Study of Terephthalic Acid in Rats. Conducted by IIT Research Institute. IITRI Study #1557, 1990.*)

4.2.2 Inhalation

The 2-hour LC_{50} in rats is greater than 2020 mg/m^3; some rats exhibited clinical signs of diarrhea, redness around nose, and discolored inguinal fur. *(Amoco Chemicals Co., Acute Inhalation Toxicity study of Purified Terephthalic Acid in Rats. Conducted by IIT Research Institute. IITRI Study #1158, 1987.)*

4.2.3 Dermal

The dermal LD_{50} in rabbits is greater than 2000 mg/kg bw and the only clinical signs noted were erythema at the application site immediately after unwrapping in 2/5 males and 4/5 females, but the animals appeared normal by Day 4. *(Amoco Chemicals Co., Acute Dermal Toxicity Study of Terephthalic Acid in Rabbits.Test Study Reference: IITRI SN 1558, TA# 445F, 1990)*

4.3 Sensitization/Irritation

In a sensory irritation (Alarie) test, the respiratory rate in mice was depressed 19% when exposed to an aerosol of 1000 mg/m^3, indicating a low irritation potential. Terephthalic acid is virtually non-irritating to the skin and eyes of rabbits. It is not a skin sensitizer to guinea pigs.

4.4 Repeated dose toxicity

4.4.1 Oral exposure

The primary adverse effect of high doses of terephthalic acid administered to rats in a 15-week study is almost completely restricted to the urinary tract. These effects include formation of bladder calculi, and inflammatory changes and hyperplasia of the bladder epithelium. Hematuria, proteinuria, body weight loss or decreased body weight gain often accompany the urinary changes. The calculi are composed primarily of a calcium-terephthalate complex, which do not occur unless the solubility of Ca^{++} and terephthalate is exceeded. The NOAEL is 1.6% terephthalic acid in the diet (which corresponds to 1220 mg/kg bw in male rats, and 1456 mg/kg in female rats). The LOAEL is 5% terephthalic acid in the diet (which corresponds to 3837 mg/kg/day in male rats and 4523 mg/kg/day in female rats). *(Amoco Corporation, Fifteen Week Oral ToxicityStudies of Terephthalic Acid – Albino Rats. Conducted by Toxicological Evaluations. LSL Study#1358, 1970)*

4.4.2 Dermal exposure

No studies found.

4.4.3 Inhalation exposure

Repeated exposure inhalation studies up to 10 mg/m^3 (6 hours/day, 5 days/week for 180 days) using rats or guinea pigs showed no adverse effects, except for mild respiratory irritation in one study with rats. *(Heck, H. d'A., and Tyl, R.W. The induction of bladder stones by terephthalic acid, dimethyl terepthalate, and melamine (2,4,6-triamino-s-triazine and its relevance to risk assessment. Regul. Toxicol. Pharmacol. 5, 294-313, 1985)*

4.5 Genotoxicity

Terephthalic acid has been extensively tested in the Ames/Salmonella assay. It was not mutagenic in the presence or absence of metabolic activation. No cytogenetic effects or micronuclei were observed when terephthalic acid was tested in an in vitro assay using human blood lymphocytes. Terephthalic acid was not clastogenic to Chinese hamster lung fibroblasts and did not induce DNA single strand breaks in rat hepatocytes. Furthermore, terephthalic acid did not induce an increase in micronucleated polychromatic erythrocytes (micronuclei) in male or female mice in vivo. *(Bioreliance, Mammalian erythrocyte micronucleus test. Study No. AA41MJ.123.BTL for BP Amoco, 2001).*

4.6 Carcinogenicity

Two-year feeding studies showed increase incidence of calculi, bladder hyperplasia and tumors in rats. These effects were seen at doses of 2% and higher terephthalic acid in the diet. The induction of bladder tumors is believed to be a result of injury to the bladder epithelium from calculi formation. (*CIIT, Chronic Dietary Administration Of Terephthalic Acid. CIIT Docket 20124, 1983)*

4.7 Reproductive/Developmental Toxicity

In a one-generation reproduction study, no adverse effects on fertility were noted in adult rats fed up to 5% terephthalic acid in the diet (approximately 2800 to 3000 mg/kg/day).

There were increased postnatal deaths on Day 1 and decreased survivability to Day 21. Several large litters of pups were lost to dams suffering obvious signs of toxicity. Several of these dams did not allow the pups to nurse or attend to the litters. Unscheduled deaths occurred during the postweaning period in the 5% groups and was associated with a very high incidence of renal and bladder calculi. Weanling animals exhibit a higher incidence of calculi compared to adults consuming the same dietary level of terephthalic acid. This can be explained by the large amount of feed consumed in relation to body weight for young animals experiencing their initial growth spurt. The NOAEL for maternal and developmental toxicity was 0.5% terephthalic acid in the diet (approximately 240 to

307 mg/kg/day). *(CIIT, A Ninety-Day Study of Terephthalic Acid (CAS No. 100-21-0) Induced Urolithiasis and Reproduction Performance in Wistar and CD Rats. CITI Docket 11622, 1982)*

Both maternal and post-natal developmental effects occurred in the 2% and 5% groups. No treatment-related maternal or fetal developmental effects was noted when female rats were exposed by inhalation up to 10 mg/m^3 terephthalic acid during days 6 through 15 of gestation. *(Ryan BM, Hatoum NS, Jernigan JD. A segment II inhalation teratology study of terephthalic acid in rats. Toxicologist 10, 40, 1990; Amoco Corporation, A Segment II Inhalation Teratology Study of Terephthalic Acid in Rats. Conducted by IIT Research Institute. IITRI Study #1448, 1989)*

4.8 Human Experience

A 10 ml application of an oily paste containing 80% terephthalic acid to equal sites on the hand was not irritating. Also, a 24-hour application did not produce any signs of irritation or redness. *(Massman, Inst Fuer Arbeitsmedizin der Uni Tuebingen, 1966)*

5.0 CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

Terephthalic acid is non-toxic to aquatic organisms at concentrations lower than its water solubility (which is 15 mg/l at 10° C). It is not expected to bioaccumulate. Terephthalic acid is subject to hydroxy radical oxidation in the atmosphere, and biodegrades in soil and surface water under aerobic conditions. Detection of terephthalic acid in air and water samples has been in the low ppt range.

Terephthalic acid is not acutely toxic, and it is virtually non-irritating to the skin and eyes. The primary adverse effect of high doses of terephthalic acid (greater than 5% in the diet) to rats is almost completely restricted to the urinary tract. These effects include formation of bladder calculi, and inflammatory changes and hyperplasia of the bladder epithelium. These urinary changes did not occur when exposure was by inhalation. Rats fed terephthalic acid (greater than 2%) for two years developed bladder calculi, bladder hyperplasia, and bladder tumors. Terephthalic acid does not appear to be genotoxic and is not metabolized by rats. Terephthalic acid is not a reproductive toxicant; however, in a one-generation reproduction feeding study, postnatal developmental effects were observed in rats. The adverse effects observed in the offspring appear to be the result of maternal toxicity and the formation of renal and bladder calculi in the weanling animals. No developmental effects were seen in rats when exposure was by inhalation.

It is believed that the calculi injure the bladder epithelium and induce cell proliferation, which is probably a critical factor in the induction of bladder tumors by terephthalic acid. Bladder calculi cannot occur unless the solubility of the stone components is exceeded (i.e., unless the product of the concentrations of Ca^{++} and terephthalate in urine exceeds the solubility product of the calcium-terephthalate complex). Based on urinary solubility of Ca-terephthalate, normal human urine would become saturated with Ca-terephthalate at a terephthalic acid concentration of approximately 8 to 16 mM. Assuming that the average volume of urine excreted by humans is 1.5 liters/day, the amount of terephthalic acid that would have to be absorbed to produce the minimum saturating concentration of terephthalic acid is 2400 mg/day. *(Heck, H. d'A., and Tyl, R.W., The induction of bladder stones by terephthalic acid, dimethyl terepthalate, and melamine (2,4,6-triamino-s-triazine and its relevance to risk assessment. Regul. Toxicol. Pharmacol. 5, 294-313, 1985.)*

Available data support a low health risk to humans. Terephthalic acid is an industrial chemical intermediate, and occupational exposures are low. It is primarily produced to make polyethylene terephthalate (PET) resins and fibers. The major end uses for PET are in consumer applications. PET containers are used for a wide variety of food and beverage packaging.

5.2 Recommendations

It is recommended that terephthalic acid be considered as low priority for further work.

6.0 REFERENCES

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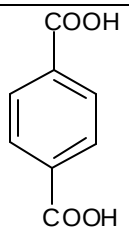
SIDS DOSSIER
(Terephthalic Acid CAS No.: 100-21-0)

SIDS PROFILE

1.01A.	**CAS NO.**	**100-21-0**
1.01C.	**CHEMICAL NAME**	TEREPHTHALIC ACID
1.01D.	**CAS DESCRIPTOR**	
1.01G.	STRUCTURAL FORMULA	
1.5	**OTHER CHEMICAL IDENTITY INFORMATION** **QUANTITY**	1,4-BENZENE-DICARBOXYLIC ACID p-PHTHALIC ACID In 1993, the worldwide production was estimated to be 17-21 billion kg.
1.7	**USE PATTERN**	Used to make polyethylene terephthalate (PET) fibers and resins, films and polyester fibers.
1.9	**SOURCES AND LEVELS OF EXPOSURE**	Terephthalic acid is manufactured as a solid or a melt by a small number of large producers using continuous, enclosed processes, with limited occupational exposure. Consumer exposure is negligible and may occur from very low concentrations of residual terephthalic acid monomer in polyethylene terephthalate used in food and beverage packaging.
ISSUES FOR DISCUSSION (IDENTIFY, IF ANY)	SIDS testing required: None	

SIDS SUMMARY DATA

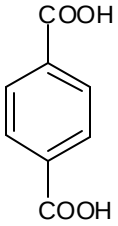
CAS NO.: 100-21-0		Information	OECD Study	GLP	Other Study	Estimation Method	Acceptable	SIDS Testing Required
STUDY		Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
PHYSICAL-CHEMICAL								N
2.1	Melting point	Y	N	N	Y	N	Y	N
2.2	Boiling point	N						N
2.3	Density	Y	N	N	Y	N	Y	N
2.4	Vapor pressure	Y	N	N	Y	N	Y	N
2.5	Partition coefficient	Y	N	N	Y	N	Y	N
2.6	Water solubility	Y	N	N	Y	N	Y	N
	pH	N						N
	pKa	Y	N	N	Y	N	Y	N
ENVIRONMENTAL FATE and PATHWAY								
3.1.1	Photodegradation	Y	N	N	N	Y	Y	N
3.1.2	Stability in water	N						
3.1.3	Stability in soil	N						
3.2	Monitoring data	Y	N	N	Y	N	Y	N
3.3	Environ. fate & Distribution	Y	N	N	N	Y	Y	N
3.5	Biodegradation	Y	Y	Y	N	N	Y	N
3.7	Bioaccumulation	Y	N	N	N	Y	Y	N
ECOTOXICITY								
4.1	Acute fish	Y	Y	Y	N	N	Y	N
4.2	Acute daphnia	Y	Y	Y	N	N	Y	N
4.3	Acute plant	Y	Y	Y	N	N	Y	N
4.4	Bacterial	Y	Y	Y	N	N	Y	N
4.5	Chronic aquatic organisms	N						N
4.6.1	Soil dwelling organisms	N						N
4.6.2	Terrestrial plants	Y	N	N	Y	N	Y	N
4.6.3	Non-mammalian species	Y	N	N	Y	N	Y	N
4.7	Biological effects monitoring	N						N
4.8	Kinetics	N						N

CAS NO.: 100-21-0		Information	OECD Study	GLP	Other Study	Estimation Method	Acceptable	SIDS Testing Required
STUDY		Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
TOXICITY								
5.1.1	Acute Oral	Y	Y	Y	N	N	Y	N
5.1.2	Acute Inhalation	Y	Y	Y	N	N	Y	N
5.1.3	Acute Dermal	Y	Y	Y	N	N	Y	N
5.1.4	Acute other routes	Y	N	N	Y	N	Y	N
5.2.1	Skin Irritation	Y	Y	N	Y	N	Y	N
5.2.2	Eye Irritation	Y	Y	N	Y	N	Y	N
5.3	Skin sensitization	Y	N	N	Y	N	Y	N
5.4	Repeated Dose	Y	N	N	Y	N	Y	N
5.5	Genetic Toxicity *in vitro*	Y	Y	Y	Y	N	Y	N
	Bacterial	Y	N	N	Y	N	Y	N
	Non-bacterial	Y	N	N	Y	N	Y	N
5.6	Genetic Toxicity *in vivo*	Y	Y	Y	N	N	Y	N
5.7	Carcinogenicity	Y	N	N	Y	N	Y	N
5.8	Reproduction Toxicity	Y	N	Y	Y	N	Y	N
5.9	Developmental toxicity	Y	N	Y	Y	N	Y	N
5.10	Toxicokinetics	Y	N	N	Y	N	Y	N
5.11	Human exposure	Y	N	N	Y	N	Y	N

1.0 General Information

1.0.1 Substance Information

A.	**CAS-Number**	100-21-0
B.	**Name** (IUPAC name):	1,4-Benzenedicarboxylic acid p-Phthalic acid
C.	**Name** (OECD name):	Terephthalic acid
D.	**CAS Descriptor**	(where applicable for complex chemicals) Not applicable in this case
E.	**EINECS-Number**	100-21-0
F.	**Molecular Formula**	$C_8H_6O_4$
G.	**Structural Formula**	(indicate the structural formula in smiles code, if available)



c1(C(=0)0)ccc(C)(=0)0)cc1

H.	**Substance Group**	(if possible, only for petroleum products, see HEDSET Explanatory note) Not Applicable
I.	**Substance Remark**	(indicate the substance remark as prescribed in the EINECS Inventory, if possible)
J.	**Molecular Weight**	166

1.0.2 OECD INFORMATION

Sponsor Country:	United States of America
Lead Organization	U.S. Environmental Protection Agency

Contact person: Dr. Oscar Hernandez
Address: Director, Risk Assessment Division
Office of Pollution Prevention & Toxics (7403)
U. S. Environmental Protection Agency
Ariel Rios Building
1200 Pennsylvania Avenue, NW
Washington, DC 20460
Telephone (202) 260-1835
Fax (202) 260-1216

Name of responder: (Information on a responder should be provided when companies respond to Lead Organization or SIDS Contact Points)

Name: David Dutton
Toxicologist

Address: BP Amoco p.l.c.
Mail Code 5A
150 West Warrenville Road
Lisle, IL 60563-8460
Tel. No. (630) 420-5079
Fax No. (630) 420-5371
E-mail:duttondr@bp.com

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance
Element [ ]; inorganic [ ]; natural substance [x]; organic [X]; Organometallic [ ]; petroleum product [ ]

B. Physical State
Gaseous [ ]; liquid [ ]; solid [X]

C. Purity (indicate the percentage by weight/weight)
>99.9% (Eastman Chemical Company)

1.2 SYNONYMS

1,4,-benzenedicarboxylic Acid
p-Phthalic acid
TPA

1.3 IMPURITIES (indicate CAS No., chemical name (IUPAC name is preferable), percentage, if possible EINECS number)

None

1.4 ADDITIVES (e.g. stabilizing agents, inhibitors, etc.)

Indicate CAS No. chemical name (IUPAC name is preferable), percentage, if possible EINECS Number, the component of the UVCB (Substance with no defined composition) should be indicated here)

None

1.5 QUANTITY:

Total annual U.S. nameplate production capacity was estimated for 1997 at 1.3 million tonnes. Total annual worldwide nameplate production capacity was estimated to be 17-21 billion kg in 1993. Total U.S. production in 1993 was estimated to be 3.8 - 4.8 billion kg.

1.6 LABELLING AND CLASSIFICATION (If possible, enter information on labeling and classification)

1.7 USE PATTERN

A. General

Type of Use: Terephthalic acid is primarily used in the manufacture and production of polyester fibers, films, polyethylene terephthalate solid state resins, and polyethylene terephthalate and polybutylene terephthalate engineering resins.

Category: Non-dispersive use; Chemical industry use as intermediate

B. Uses in Consumer Products:

Polyester fibers accounts for a majority of terephthalic acid use. End products of polyester fiber may include yarns for carpet, apparel, fill fibers for consumer products, and industrial filaments. Polyethylene terephthalate solid state resins are the next most common use and are used primarily for food and beverage containers. Remaining uses include polyester films, such as photographic films and magnetic tape base, polyethylene terephthalate engineering resins, and polybutlyene terephthalate engineering resins used primarily in automobile parts. Also some terephthalic acid may be converted to dimethylterephthalate.

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

ACGIH: 10 mg / m^3 8-hour TLV

1.9 SOURCES OF EXPOSURE

Terephthalic acid is manufactured as a solid or a melt by a small number of large producers using continuous, enclosed processes, with limited occupational exposure. Consumer exposure is negligible and may occur from very low concentrations of residual terephthalic acid monomer in polyethylene terephthalate used in food and beverage packaging.

2.0 PHYSICAL-CHEMICAL DATA

2.1 MELTING POINT

Melting Point:	> 300° C
Method:	
GLP:	Yes [ ] No [X]
Comments:	Information predates GLP regulations
Reference:	Bemis, Dindorf, Harwood, Samans. (1982) Kirk-Othmer Encyclopedia of Chemical Technology 3rd Ed Vol 17, 734

Melting Point:	402° C
Method:	
GLP:	Yes [ ] No [X]
Comments:	Information predates GLP regulations
Reference:	Anon (1988) Dangerous Properties of Industrial Materials Report 8, 68-71

Melting Point:	425^0 C
Method:	
GLP:	Yes [ ] No [X]
Comments:	Measured in sealed tube. Information predates GLP regulations
Reference:	ICI Chemicals & Polymers Limited Product Safety Data: Pure Terephthalic Acid, Jan 1991

2.2 BOILING POINT

Not available

2.3 DENSITY

Type:	Bulk density
Value:	1.12 g/cm^3
Method:	Other: DIN 5314
GLP:	Unknown
Reference:	ICI Chemicals & Polymers Limited Product Safety Data: Pure Terephthalic Acid, Jan 1991

Type:	Density
Value:	1.5 g/cm^3
Method:	Other
GLP:	Unknown
Reference:	ICI Chemicals & Polymers Limited Product Safety Data: Pure Terephthalic Acid, Jan 1991

Type:	Density
Value:	1.51 g/cm^3
Method:	Other
GLP:	Unknown
Reference:	Anon (1988) Dangerous Properties of Industrial Materials Report 8, 68-71

2.4 VAPOUR PRESSURE

Vapour Pressure at 20^0 C: **$3x10^{-10}$ hPa**
Method:
GLP: Unknown
Comment: Value extrapolated from vapor pressures measured at temperatures between 250 and 427^0 C.
Reference: Daubert, Danner. (1983) Data Compilation Tables of Properties of Pure Comp., AICHE/DIPPR

Vapour Pressure at 20^0 C: **$3x10^{-11}$ hPa (extrapolated)**
Method:
GLP: Unknown
Comment:
Reference: Verschueren Handbook of Environmental Data on Organic Chemicals, 3rd Ed.

Vapour Pressure at 25^0 C : **$1.19x10^{-5}$ mm Hg (calculated)**

Method:
GLP: Unknown
Comment: Estimated value using MPBPWIN model, v 1.40
Reference: Syracuse Research Corporation, Syracuse, NY

Vapour Pressure at 78^o C: 1.33 hPa
Method:
GLP: Unknown
Reference: West RC. (1969) CRC Handbook of Chemistry and Physics 50th Edn CRC Press Inc., Cleveland Ohio

Vapour Pressure at 304^0 C: 13 hPa
Method:
GLP: Unknown
Reference: ICI Chemicals & Polymers Limited Product Safety Data: Pure Terephthalic Acid, Jan. 1991

2.5 PARTITION COEFFICIENT

Partition Coefficient: log P= 1.16
Method:
GLP: Unknown
Reference: Church C. Unpublished analysis Zeneca Brixham Environmental Laboratory

Partition Coefficient: log P= 1.19
Method:
GLP: Unknown
Reference: Leo, A.J. (1978) Report on the calculation of octanol/water log P valves for structures in EPA files

Partition Coefficient: log P= 1.25 at 25^0 C
Method:
GLP: Unknown
Reference: Tomida, Yotsiyanag, Ikeda. (1978): Chem Pharm Bull 261, 2824-2831, Verschueren Handbook of Environmental Data on Organic Chemicals, 3rd Ed.

Partition Coefficient: log P= 1.96
Method:
GLP: Unknown

Reference: Dunn, Johnson. (1983) Plank Struct Act Relat 2 156-163, Verschueren Handbook of Environmental Data on Organic Chemicals, 3rd Ed

Partition Coefficient: log P= 2 (measured)
Method:
GLP: Unknown
Reference: (1) Chan, Hansch: Pomona College (unpublished); 2 cited in: Hansch, Leo (1985): Pomona College Medicinal Chemistry Data base. (2) Verschueren Handbook of Environmental Data on Organic Chemicals, 3rd Ed. Hansch, Leo, Hoekman. (1995) Exploring QSAR, American Chemical Society

2.6 WATER SOLUBILITY

Solubility: 15 mg/l at 10° C (not soluble)
Method:
GLP: Unknown
Reference: ICI Chemicals & Polymers Limited Product Safety Data: Pure Terephthalic Acid Jan 1991

Solubility: 15 mg/l at 20 ° C (not soluble)
Method:
GLP: Unknown
Reference: Arizona Database

Solubility: 19 mg/l at 25° C (not soluble)
Method:
GLP: Unknown
Reference: Bemis, Dindorf, Harwood, Samans. (1982) Kirk-Othmer Encyclopedia of Chemical Technology 3rd Ed Vol 17, 734

pKa VALUE:
pKa1= 3.52 at 25^0 C
Method:
GLP: Unknown
Reference: Bemis, Dindorf, Harwood, Samans. (1982) Kirk-Othmer Encyclopedia of Chemical Technology 3rd Ed Vol 17, 734

pKa1= 4.46 at 25^0 C
Method:
GLP: Unknown
Reference: Bemis, Dindorf, Harwood, Samans. (1982) Kirk-Othmer Encyclopedia of Chemical Technology 3rd Ed Vol 17, 734

2.7 FLASH POINT

Flash Point: 271^0 C (520° F)
Method: MicroCleveland and open cup
GLP: no
Comment: Obtained from Eastman MSDS

Flashpoint: 260° C
Method: Open Cup
GLP: Unknown
Reference: Supplement to the 6th Edition, Documentation of the Threshold Limit Values and Biological Exposure Indices. (1996)

2.8 AUTO FLAMMABILITY:

Not Available

2.9 FLAMMABILITY:

Not Available

2.10 EXPLOSIVE PROPERTIES

Explosion Limit:	0.05 g/l
Method:	
GLP: Unknown	
Reference:	Supplement to the 6th Edition, Documentation of the Threshold Limit Values and Biological Exposure Indices. (1996)

2.11 OXIDIZING PROPERTIES:

Not Available

2.12 ADDITIONAL REMARKS

Lower flammable limit:	40 g/m^3
Flammable powder class:	A
Minimum ignition temperature:	500^0 C
Minimum ignition energy:	50 mJ
Sublimation temperature:	300^0 C
Reference:	ICI Chemicals & Polymers Limited Product Safety Data: Pure Terephthalic Acid, Jan 1991

3.0 ENVIRONMENTAL FATE AND PATHWAY

3.1 STABILITY

3.1.1 PHOTODEGRADATION

Type:	air
Light source:	other
Indirect photolysis:	
Sensitizer:	OH radical
Conc. of sens.:	1.5×10^{6} OH/cm^{3}
Rate constant:	$k = 1.2370 \times 10^{-12}$ cm3/molecule-sec
Method:	other:calculated
Year:	2001
GLP:	no
Test substance:	as prescribed by 1.1-1.4
Result:	Half-life = 8.647 days
Test condition:	The rate constant at 25 degrees C was estimated using version 1.90 of the Atmospheric Oxidation Program (AOPWIN) for Microsoft Windows that estimates the rate constant for the atmospheric gas-phase reaction between photochemically produced hydroxyl radicals and ozone with organic chemicals. The rate constant estimated by the program was used to calculate the atmospheric half-life for terephthalic acid based upon the average atmospheric concentration of hydroxyl radicals.
Remark:	No ozone reaction estimation was noted. MPBPWIN v1.40 estimated the vapor pressure to be 1.19×10^{-5} mmHg (25 ^{o}C). Therefore, volatilization is unlikely to occur.
Reliability:	(2) reliable with restrictions. Value is an estimation by an accepted method.
Reference:	Syracuse Research Corporation, Syracuse, NY

3.1.2 STABILITY IN WATER:

Not Available

3.1.3 STABILITY IN SOIL:

Not Available

3.2 MONITORING DATA (ENVIRONMENT)

Type of Measurement:	
Other:	Air
Comments:	In Japan, the atmospheric concentration of terephthalic acid was 11.1 ng TPA/m^{3} (average of 6 days). The maximum value was 23 ng/m^{3}. Terephthalic acid was probably from photochemical reactions of hydrocarbons.
Reference:	Satsumabayashi, Kurita, Yokouchi, Ueda. (1990): Atmospheric Environment 24A, 1443-1450

Type of Measurement:	
Other:	River
Comments:	The maximal concentration of terephthalic acid in river water in Japan (1975) was 3.4 ug/l.
Reference:	Matsumoto (1982): Water Res. 16, 551-557

Type of Measurement:	
Other:	Sewage plant drainage
Comments:	The terephthalic acid concentration was approximately 13 ng/l from drainage of a sewage plant in Washington D.C. (1975)

Reference: Lin, Melton, Kopfler, Lucas. (1981): Advances in the Identification & Analysis of Organic Pollutants in Water; Volume 2 edited by L.H. Keith, 861-906

Type of Measurement:
Other: Sewage plant drainage
Comments: The terephthalic acid was 5.3 ug/l in a sewage plant drain in Japan (1975).
Reference: Matsumoto (1982): Water Res. 16, 551-557

Type of Measurement:
Other: Sludge
Comments: In W. Germany (1984), terephthalic acid was detected in sludge from a local sewage plant.
Reference: Anna, Ploeger, Reupert. (1984): Gewaesserschutz, Wasser, Abwasser 65, 315-331

Type of Measurement:
Other: Sea coast
Comments: In Japan, terephthalic acid was found in 6 out of 10 sea water samples with an average concentration of 0.7 ug/l. The samples were taken between 1974 and 1976 from an industrial coastal area.
Reference: Kubota. (1979): Ecotoxicol. Environ. Safety 3, 256-268

Type of Measurement:
Other: Plants
Comments: Terephthalic acid is naturally found in Kreuzdorngewaechsen (Rhamnaceae, Zizyphus sativa).
Reference: Thakur, Jain, Hruban, Santavy. (1975): Planta Med. 28, 172-173

3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.1 TRANSPORT

Type: Theoretical distribution
Media: ther: air, water, soil, sediment
Air (level III): 0.000012%
Water (level III): 32.7%
Soil (level III): 67.2%
Sediment (level III): 0.098%
Method: Other:calculation
Year: 2001
GLP: No
Test substance: As prescribed by 1.1-1.4
Test condition: Level III Fugacity was estimated using the Mackay model (the currently accepted model for estimation of theoretical distribution) with standard defaults contained in Syracuse Research Center EPIWIN version 3.05 and a M.W of 166.13, Log K_{ow} of 2.00 (experimental database match), vapor pressure (mmHg, 25°C) of 1.19 x 10^{-5}, water solubility (20°C) of 15 mg/l (experimental database match),
Henry's Law Constant of 2.071 x 10^{-9} atm-m^3/mole (HENRYWIN v3.10), and a Soil log K_{oc} of 1.855 (PCKOCWIN v1.66).
Conclusion: This material is expected to distribute primarily into soil and water.
Reliability: (2) reliable with restrictions. Value is an estimation by an accepted method.
Reference: Syracuse Research Corporation, Syracuse, NY

3.3.2 DISTRIBUTION:

Not Available

3.4 MODE OF DEGRADATION IN ACTUAL USE:

Not Available

3.5 BIODEGRADATION

Type:	Aerobic		
Inoculum:	Activated sludge		
Contact time:	16 days		
Degradation:	85.2% (10 mg/l) 82.6% (20 mg/l)		
Result:	Readily biodegradable		
Kinetic of test substance:	2 days = 15.5% (10 mg/l)	34.3%	(20 mg/l)
	5 days = 68.2%	66.0%	
	7 days = 70.4%	68.7%	
	12 days = 77.4%	75.1%	
	16 days = 85.2%	82.6%	
Deg. Product:	CO_2		
Method:	OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test		
Year:	1991		
GLP:	Yes		
Test substance:	As prescribed by 1.1-1.4		
Remark:	Terephthalic acid was supplied by the Amoco Corporation. Purity was not noted but typically exceeds 99%.		
Result:	>83% of the theoretical CO_2 evolution occurred within 16 days. The test was validated by use of a positive control (Na-Benzoate) that was degraded by 77% within approximately 6 days.		
Test condition:	Inoculum was obtained from a domestic sewage plant not treating industrial wastes. It was washed with tap water, and resolubilized and aerated prior to use. Degradation of test article was assessed at concentrations of 10 and 20 mg/l using a guideline mineral salt solution. The final total test volume was 3500 ml. Test solutions were stirred with magnetic stirrers. A test blank and a positive control (Na-Benzoate) were run simultaneously. Degradation was determined by the capture of generated CO_2. The study was conducted in the dark at a temperature range of 22.0-23.5 °C. The system was aerated at a rate of 4 L/h.		
Remark:	The test method is applicable only with a material that has a negligible vapor pressure at the levels utilized in this study, is not inhibitory to bacteria, and does not absorb to glass surfaces The test was scheduled for 28 days but was stopped after the degradation curve reached an early plateau.		
Reliability:	(1) reliable without restriction		
Reference:	Amoco Corporation (1991). Study on the Ready Biodegradability (Modified Sturm Test) of Terephthalic Acid; Conducted by Battelle Europe; Study # BE-EA-128-91-01-STT-03		

Type:	Aerobic
Inoculum:	Activated sludge, adapted
Degradation:	72 % after 28 days
Method:	OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO_2 evolution)"
GLP:	Unknown
Test Substance:	No Data
Comments:	Conducted in accordance with the 1973 proposed Sturm method.
Reference:	Gerike, Fischer. (1979): Ecotoxicol. Environ. Safety 3, 159- 173

Type:	Aerobic
Inoculum:	Activated sludge, adapted
Degradation:	91 % after 28 days

Method: OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO_2 evolution)"
GLP: Unknown
Test Substance: No Data
Comments: Conducted in accordance with the 1973 proposed Sturm method.
Reference: Gerike, Fischer. (1979): Ecotoxicol. Environ. Safety 3, 159-173

Type: Aerobic
Inoculum: Domestic sewage, non-adapted
Concentration: 20 mg/l related to Test substance
Degradation: > 60 % after 10 days
Result: Biodegradable
Method: OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO_2 evolution)"
GLP: Yes
Test Substance: As prescribed by 1.1 - 1.4
Comments: A value of >60% degradation was also obtained with a nominal initial concentration of 10mg/l terephthalic acid.
Reference: Amoco Chemicals Co. (1992) Data cited in a letter with enclosures from Amoco Chemicals Co. to ICI Chemicals & Polymers Limited. Dated January 29, 1993

Type: Aerobic
Inoculum: Activated sludge, non-adapted
Degradation: After 30 days
Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
GLP: Unknown
Test Substance: No Data
Comment: Conducted in accordance with the 1974 Standard method. The degree of degradation was 112% at 30 days.
Test condition: 1 drop/l
Reference: Gerike, Fischer. (1979): Ecotoxicol. Environ. Safety 3, 159-173

Type: Aerobic
Inoculum:
Other: Schluffinger clay
Concentration: 20 mg/l related to test substance
Degradation: 100 % after 2 days
Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
GLP: Unknown
Test Substance: No Data
Reference: Alexander M, Lustigman BK. (1966) Effect of chemical structure on microbial degradation of substituted benzenes. J Agric Food Chem 14, 410-3

Type: Aerobic
Inoculum: Predominantly domestic sewage
Degradation: 82 % after 19 days
Method: OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
GLP: Unknown
Test Substance: No Data
Comment: Conducted according to the proposed 1976 OECD method.
Reference: Gerike, Fischer. (1979): Ecotoxicol. Environ. Safety 3, 159-173

Type: Aerobic
Inoculum: Activated sludge, industrial, non-adapted
Concentration: Related to test substance
Degradation: 98 % after 6 days
Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"

GLP: Unknown
Test Substance: No Data
Reference: Wellens. (1990): Z. Wasser-Abwasser Forsch. 23, 85-98

Type: Aerobic
Inoculum: Activated sludge, non-adapted
Degradation: 93 % after 4 days
Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
GLP: Unknown
Test Substance: No Data
Reference: Gerike, Fischer. (1979): Ecotoxicol. Environ. Safety 3, 159-173

Type: Aerobic
Inoculum: Activated sludge, non-adapted
Degradation: 93 % after 1 day
Method: OECD Guide-line 303 A "Simulation Test - Aerobic Sewage Treatment: Coupled Unit Test"
GLP: Unknown
Test Substance: No Data
Comment: Conducted according to the 1976 OECD Confirmatory Test Stand Method.
Reference: Gerike, Fischer. (1979): Ecotoxicol. Environ. Safety 3, 159-173

Type: Aerobic
Inoculum: Activated sludge
Concentration: 1000 mg/l related to Test substance
Degradation: 30 - 100 % after 14 days
Result: Other
Method: Other
GLP:
Test Substance:
Comment: 30 mg/l Activated Sludge
Method: Japanese MITI
Temperature: 25° C
Reference: Kitano M. (1978) Biodegradation and bioaccumulation test on chemical substances. OECD Tokyo meeting reference book TSU -No 3

Type: Aerobic
Inoculum: Activated sludge
Concentration: 100 mg/l related to Test substance
Degradation: 30 - 100% after 14 days
Result: Other
Method: Japanese MITI
GLP: Unknown
Test Substance: Other TS
Comment: 30 mg/l Activated Sludge
Temp: 25° C pH 7.0
Reference: Sasaki S. (1978) The scientific aspects of the chemical substance control law in Japan. In: Aquatic Pollutants: Transformation and Biological effects. Hutzinger O., Von Letoeld L.H., and Zoetman B.C.J. (Eds) Oxford Pergamon Press 283-98

Type: Aerobic
Inoculum: Activated sludge
Degradation: 72 %
Result: Other
Method: Sturm
GLP: Unknown
Test Substance: Other TS
Results: CO_2 evolved

Reference: Gerike P, Fischer WK. (1979) A correlation study of biodegradability determinations with various chemicals in various tests. Ecotox Environ Safety 3, 159-73.

Type: Aerobic
Inoculum: Activated sludge
Degradation: 82 % and 91 %
Method: OECD Screening test
GLP: Unknown
Reference: Gerike P, Fischer WK. (1979) A correlation study of biodegradability determinations with various chemicals in various tests. Ecotox Environ Safety 3, 159-73.

Type: Aerobic
Inoculum: Activated sludge
Degradation: 93 % after 4 days
Method Zahn-Wellens % DOC removal; Coupled units
GLP:
Test substance:
Reference: Gerike P, Fischer WK. (1979) A correlation study of biodegradability determinations with various chemicals in various tests. Ecotox Environ Safety 3, 159-73.

Type: Aerobic
Inoculum: Activated sludge
Method: Closed bottle
GLP: Unknown
Test Substance: Other TS
Results: % BOD
Reference: Gerike P, Fischer WK. (1979) A correlation study of biodegradability determinations with various chemicals in various tests. Ecotox Environ Safety 3, 159-73.

Type: Aerobic
Inoculum: Activated sludge
Concentration: 100 mg/l related to test substance
Result: Other
Method: Other
GLP: Unknown
Test Substance: Other TS
Comment: Degraded in 2 weeks Temp: 25° C
Reference: Kitano M. (1978) Biodegradation and bioaccumulation test on chemical substances. OECD Tokyo meeting Reference book TSU-No 3

Type: Aerobic
Concentration: 20 mg/l related to test substance
Degradation: 100% after 2 days
Method: Other
GLP: Unknown
Test Substance: Other TS
Comment: Soil inoculum from niagara silt loam
Medium: Soil and mineral salts
Reference: Alexander M, Lustigman BK. (1966) Effect of chemical structure on microbial degradation of substituted benzenes. J Agric Food Chem 14, 410-3

Type: Aerobic
Inoculum: Other
Concentration: 40 mg/l related to Test substance
Degradation: 66 % after 28 days
Result: Other
Method: Other
Year: 1981

GLP: Unknown
Test Substance: Other TS
Remark:
Method: French AFNOR % Doc removal
Inoculum: 5 x 10^5 germs/ml
Reference: Gerike P, Fischer WK. (1979) A correlation study of biodegradability determinations with various chemicals in various tests. Ecotox Environ Safety 3, 159-73.

Type: Aerobic
Inoculum: Other
Concentration: 40 mg/l related to test substance
Degradation: 66 % after 42 days
Result: Other
Method: Other
Year: 1981
GLP: Unknown
Test Substance: Other TS
Remark:
Method: French AFNOR % Doc removal
Inoculum: 5 x 10^5 germs/ml
Reference: Gerike P, Fischer WK. (1979) A correlation study of biodegradability determinations with various chemicals in various tests. Ecotox Environ Safety 3, 159-73.

Type: Aerobic
Inoculum: Other
Degradation:
Result: Other
Method: Other
Year: 1978
GLP: Unknown
Test Substance: Other TS
Remark:
Test Param: Degradation in natural ecosystems
Method: MITI
Result: Confirmed to be significantly degraded
Reference: Sasaki S. (1978) The scientific aspects of the chemical substance control law in Japan. In: Aquatic Pollutants: Transformation and Biological effects Hutzinger O, Von Letoeld L.H. and Zoetman B.C.J. (Eds) Oxford Pergamon Press 283-98

Type: Aerobic
Inoculum: Other
Degradation:
Result: Other
Method: Other
Year: 1983
GLP: Unknown
Test Substance: Other TS
Remark:
Inoculum: Soil bacteria
Results: Decomposes in 2 days.
Reference: Verschueren K. (1983) Handbook of environmental data on organic chemicals (2nd Edition) Van Nostrand Reinhold

Type: Aerobic
Inoculum: Other
Concentration: 3000 mg/l related to test substance
Degradation:
Result: Other
Method: Other
Year: 1977

GLP: Unknown
Test Substance: Other TS
Remark:
Inoculum: Pseudomonas acidovorans
Results: Degraded in 30 days
Medium: Mineral salts
Reference: Kurane R, Suzuki T, Takahara Y. (1977) Microbial degradation of phthalate esters. Part I. Isolation of microorganisms growing on phthalate esters and degradation of phthalate esters by pseudomonas acidovorans 256-1 Agric Biol Chem 41, 2119-23

Type: Aerobic
Inoculum: Other
Degradation:
Result: Other
Method: Other
Year: 1976
GLP: Unknown
Test Substance: Other TS
Remark: Microbes (various pure cultures including P Testosteroni) isolated by enrichment from soil, plant debris, fresh and brackish water and raw sewage.
Result: Degrades
Reference: Keyser P, Pujar BG, Eaton RW, Ribbons DW. (1976) Biodegradation of the phthalates and their ester by bacteria. Environ Health Perspect 18, 159-66

Type: Aerobic
Inoculum: Other
Degradation:
Result: Other
Method: Warburg Respirometer
Year: 1981
GLP: Unknown
Test Substance:
Remark: The medium was a mixed culture of bacteria isolated from freshwater sediment grown aerobically and anaerobically on test compound, but not other phthalic isomers. The temperature was 30 degrees C and the pH was 7.5.
Result: Degraded after lag.
Reference: Aftring RP, Chalker BE, Taylor BF. (1981) Degradation of phthalic acids by denitrifying mixed cultures of bacteria. Appl Environ Microbiol 41, 1177-83

Type: Aerobic
Inoculum: Pseudomonas sp. (Bacteria)
Concentration: 2000 mg/l related to DOC (Dissolved Organic Carbon)
Degradation:
Method:
Other: Ultimate biodegradation
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from mold using an aerobic enrichment medium of o-phthalic acid. Can grow in an aqueous medium containing terephthalic acid as the sole energy and carbon source.
Reference: Nozawa, Maruyama. (1988): J. Bacteriol. 170, 5778-5784

Type: Aerobic
Inoculum: Activated sludge, non-adapted
Concentration: 100 mg/l related to test substance
Degradation:
Method:

Other: MITI-Test
Year:
GLP: Unknown
Test Substance: No Data
Remark: The duration was presumably 14 days. The degree of degradation in aqueous medium was not cited; however, the test substance was considered classified as biodegraded.
Reference: Kubota. (1979): Ecotoxicol. Environ. Safety 3, 256-268

Type: Aerobic
Inoculum: Other bacteria:
Concentration: 3.3 mg/l related to
Degradation:
Method:
Other: O_2-receptor, pH = 8
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from the bacteria from seabed sediment. Grown in aqueous medium containing terephthalic acid as the sole energy and carbon source.
Reference: Taylor, Amador. (1988): Appl. Environ. Microbiol. 54, 2342-2344

Type: Aerobic
Inoculum: Nocardia sp.
Concentration: 4000 mg/l related to test substance
Degradation: ca. 100 % after 110 hour
Method:
Other: Increase in turbidity at 578 nm; pH = 7.2
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from soil with an enrichment culture containing phthalic acid.
Reference: Engelhardt, Wallnoefer, Rast (1976): Arch. Microbiol. 109, 109-114

Type: Aerobic
Inoculum: Bacillus cirroflagellosus (Bacteria)
Concentration: Related to test substance
Degradation:
Method:
Other: Increase in turbidity at 660 nm
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from mold. Can grow in aqueous medium containing terephthalic acid as the sole energy and carbon source. Concentrations used: 500 to 2000 mg/l
Reference: Karegoudar, Pujar. (1984): Proc. Indian Acad. Sci. (Chem. Sci.) 93, 1155-1158

Type: Aerobic
Inoculum: Other bacteria: Bacillus sp.
Concentration: 2000 mg/l related to test substance
Degradation: = 100 % after 1 day
Method:
Other: Increase in turbidity at 660 nm
Year:
GLP: Unknown
Test substance: No Data
Remark: Isolated from mold.
Reference: Karegoudar, Pujar. (1985): FEMS Microbiol. Lett. 30, 217-220

Type: Aerobic
Inoculum: Pseudomonas sp. (Bacteria)

Degradation:
Method:
Other: Increase in turbidity at 660 nm
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from mold. Grown in an enrichment culture containing an aqueous media of terephthalic acid as the sole energy and carbon source.
Reference: Nozawa, Maruyama. (1988): J. Bacteriol. 170, 2501-2505

Type: Aerobic
Inoculum: Alcaligenes sp. (Bacteria)
Degradation:
Method:
Other: Unknown
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from soil using phthalic acid in the growth medium. Grown in enrichment culture with terephthalic acid as the sole energy and carbon source.
Reference: Harada, Koiwa. (1977): J. Ferment. Technol. 55, 97-102; cited in: Chem. Abstr. 87, 2191h (1977)

Type: Aerobic
Inoculum: Alcaligenes sp. (Bacteria)
Degradation:
Method:
Other: Unknown
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from soil. Grown in enrichment culture with terephthalic acid as the sole energy and carbon source.
Reference: Koiwa, Igatashi. (1979): Toyo Soda Kenkyu Hokoku 23, 35-39; cited in: Chem. Abstr. 90, 182922r (1979)

Type: Aerobic
Inoculum: Arthrobacter sp. (Bacteria)
Degradation:
Method:
Other: Unknown
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from soil using iso-phthalic acid in the isolation medium. Grown in medium with terephthalic acid as the sole energy and carbon source.
Reference: Harada, Koiwa. (1977): J. Ferment. Technol. 55, 97-102; cited in: Chem. Abstr. 87, 2191h (1977)

Type: Aerobic
Inoculum: Arthrobacter sp. (Bacteria)
Degradation:
Method:
Other:
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from soil using and aqueous medium containing terephthalic acid as the sole energy and carbon source.
Reference: Koiwa, Igatashi. (1979): Toyo Soda Kenkyu Hokoku 23, 35-39; cited in: Chem. Abstr. 90, 182922r (1979)

Type: Aerobic
Inoculum: Arthrobacter terregens (Bacteria)
Degradation:
Method:
Other: Unknown
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from an industrial sewage pond with terephthalic acid in the isolation medium. Grown in medium containing an aqueous medium of terephthalic acid as the sole energy and carbon source.
Reference: Karegoudar, Pujar. (1984): J. Karnatak Univ. Sci. 29, 69-73; cited in: Chem. Abstr. 104, 39094z (1986)

Type: Aerobic
Inoculum: Arthrobacter terregens (Bacteria)
Degradation:
Method:
Other: Unknown
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from mold. Grown in an aqueous medium containing terephthalic acid as the sole energy and carbon source.
Reference: Karegoudar, Pujar. (1984): Proc. Indian Acad. Sci. (Chem. Sci.) 93, 1155-1158

Type: Aerobic
Inoculum: Bacillus cirroflagellosus (Bacteria)
Degradation:
Method:
Other: Unknown
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from an industrial sewage pond with terephthalic acid in the isolation media. Grown in an aqueous media of terephthalic acid as the sole energy and carbon source.
Reference: Karegoudar, Pujar. (1984): J. Karnatak Univ. Sci. 29, 69-73; cited in: Chem. Abstr. 104, 39094z (1986)

Type: Aerobic
Inoculum: Nocardia resticta (Bacteria)
Degradation:
Method:
Other: Unknown
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from an industrial sewage pond with terephthalic acid in the isolation media. Grown in an aqueous media of terephthalic acid as the sole energy and carbon source.
Reference: Karegoudar, Pujar. (1984): J. Karnatak Univ. Sci. 29, 69-73; cited in: Chem. Abstr. 104, 39094z (1986)

Type: Aerobic
Inoculum: Nocardia resticta
Concentration: Related to test substance
Degradation:
Method:
Other: Unknown
Year:
GLP: Unknown

Test Substance: No Data
Remark: Isolated from mold. Grown in aqueous media containing terephthalic acid as the sole energy and carbon source. Concentration: 500 to 2000 mg/l.
Reference: Karegoudar, Pujar. (1984): Proc. Indian Acad. Sci. (Chem. Sci.) 93, 1155-1158

Type: Aerobic
Inoculum: Pseudomonas alcaligenes
Degradation:
Method:
Other: Unknown
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from and industrial sewage pond with isolation media containing only terephthalic acid. Grown in aqueous media containing terephthalic acid as the sole energy and carbon source.
Reference: Karegoudar, Pujar. (1984): J. Karnatak Univ. Sci. 29, 69-73; cited in: Chem. Abstr. 104, 39094z (1986)

Type: Aerobic
Inoculum: Pseudomonas alcaligenes
Degradation:
Method:
Other: Unknown
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from mold. Grown in media containing terephthalic acid as the sole energy and carbon source. Concentration: 500 to 2000 mg/l.
Reference: Karegoudar, Pujar. (1984): Proc. Indian Acad. Sci. (Chem. Sci.) 93, 1155-1158

Type: Aerobic
Inoculum: Pseudomonas sp.
Degradation:
Method:
Other: Unknown
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from soil. Aerobic degradation in aqueous media. Grown in media containing terephthalic acid as the sole energy and carbon source.
Reference: Elmorsi, Hopper. (1981): Biochem. Soc. Trans. 9, 431

Type: Aerobic
Inoculum: Pseudomonas testosteroni
Degradation:
Method:
Other: Unknown
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated with o-phthalate as the sole carbon source. Grown aerobically in media in which terephthalic acid is the sole energy and carbon source.
Reference: Keyser, Pujar, Eaton, Ribbons (1976): Environ. Health Perspect. 18, 159-166

Type: Aerobic
Inoculum:
Other Bacteria: Acinetobacter sp.
Concentration: 200 mg/l related to Test substance

Degradation: ca. 100 %
Method:
Other: Unknown
Year:
GLP: Unknown
Test Substance: No Data
Reference: Ling, Xiong, Qian (1986): Huanjing Huaxue 5(4), 7-13; cited in: Chem. Abstr. 106, 37903e (1987)

Type: Aerobic
Inoculum: Other bacteria: Mycobacter lacticolum
Degradation:
Method:
Other: Unknown
Year:
GLP: Unknown
Test Substance: No Data
Remark: Isolated from activated sludge from an industrial site. Aerobically degrades in aqueous media containing terephthalic acid.
Reference: Naumova, Usmanova, Lisin, Shchurov (1984): Biol. Nauki (Moscow) 2, 96-100; cited in: Chem. Abstr. 100, 161361s (1984)

Type: Aerobic
Inoculum: Pseudomonas sp.
Concentration: 200 mg/l related to test substance
Degradation:
Method: Other: unknown
Year:
GLP: Unknown
Test substance: No Data
Remark: 100% degradation by 14 hours in aqueous media. Isolated from activated sludge from an industrial site. Aerobic degradation.
Reference: Ling, Xiong, Qian (1986): Huanjing Huaxue 5(4), 7-13; cited in: Chem. Abstr. 106, 37903e (1987)

Type: Anaerobic
Inoculum: Other
Degradation:
Result: Other
Method: Warburg respirometer
Year: 1981
GLP: Unknown
Test substance:
Remark: Mixed culture of bacteria isolated from freshwater sediment. Dose of 10 umol at a temperature of 30 degrees C and a pH of 7.5. Rapid degradation.
Reference: Aftring RP, Chalker BE, Taylor BF. (1981) Degradation of phthalic acids by dentrifying mixed cultures of bacteria. Appl Environ Microbiol 41, 1177-83

Type:
Inoculum: Activated sludge, non-adapted
Degradation: 0 % after 14 days
Method: Other: ORIGINAL-MITI-Test, Biodegradability and Bioaccumulation Test of Chemical Substances (C-5/98/JAP) 1978
Year:
GLP: Unknown
Test substance: No Data
Reference: Gerike, Fischer. (1979): Ecotoxicol. Environ. Safety 3, 159-173

3.6 BOD-5, COD or BOD-5/COD

Type:	Aerobic
Inoculum:	Activated sludge, adapted
Concentration:	1000 mg/l related to COD (Chemical Oxygen Demand)
Degradation:	96 % after 0.6 day
Result:	Other
Method:	Other
Year:	1984
GLP:	
Test Substance:	
Remark:	
Method:	Warburg Respirometer pH:7.0-7.2
Temperature:	30° C; Activated sludge acclimated using 1000 mg/l COD of Terephthalate in a SOAS unit for 24 days.
Reference:	Lund FA, Rodriguez DS. (1984) Acclimation of activated sludge to mono-substituted derivations of phenol and benzoic acids. J Gen Appl Microbiol 30, 53-61

Type:	Aerobic
Inoculum:	Activated sludge, adapted
Concentration:	1000 mg/l related to COD (Chemical Oxygen Demand)
Degradation:	> 95 % after 2 days
Method:	
Other:	CSB-measurement, pH 7.0 - 7.2
Year:	
GLP:	Unknown
Test Substance:	No Data
Remark:	Adapted for 24 hours. Aerobic degradation in aqueous medium.
Reference:	Lund, Rodriguez. (1984): J. Gen. Appl. Microbiol. 30, 53-61

3.7 BIOACCUMULATION

Species:	
Exposure period:	
Concentration:	
BCF:	
Elimination:	
Method:	Other
Year:	1988
GLP:	Unknown
Test substance:	
Remark:	Result: BCF = 3.2 (calculated from EPIWIN)
Reference:	Syracuse Research Corporation

3.8 ADDITIONAL REMARKS

None

4.0 ECOTOXICITY

4.1 ACUTE AND PROLONGED TOXICITY TO FISH

Type	static
Species/Strain	Golden orfe (*Leuciscus idus melanotus*)
Exposure period	96 hours
Unit	mg/l
Analytical monitoring	yes
LC0	> 1000 (nominal)
LC50	> 1000
NOEC	≥ 1000 (nominal)
Method	OECD Guideline 203 "Fish, Acute Toxicity Test"
Year	1991
GLP	yes
Test substance	as prescribed by 1.1-1.4
Remark	Terephthalic acid was supplied by the Amoco Corporation. Purity was 99.9%.
Result	Dissolved oxygen, temperature, conductivity, alkalinity, and hardness did not vary between groups. The pH of the water decreased slightly as a function of time and increasing concentration of test material (i.e. the pH of the vessel containing 1000 mg/l at 96 hours was 7). All test condition values were within acceptable limits. No mortalities or behavioral changes were noted at any concentration during the study.
Test condition	Fish were held for 21 days in 376 liter glass vessels containing 327 liters of reconstituted water (19 °C, 85-95% oxygen). Fish density was 0.51 g/liter. They were fed five times a week with 50% Tetra Special Mix and 50% IBL Novo food tablets prior to study. The study was conducted in 16 liter stainless steel vessels that contained 10 liters of test solution. Test solution was not renewed. At the time of the test, fish were an average of 4.86 ± 0.47 cm in length and weighed 1.028 ± 0.246 g. Ten fish were placed in each vessel (for a loading rate of 1.028 g/l). Fish were not fed during the test. The test article was diluted with reconstituted purified water to yield nominal concentrations of 130, 220, 350, 600 and 1000 ppm. The actual concentration of the highest exposure level was 999.3 ppm at time 0, and 922.2 ppm at 96 hours. Fish were maintained at 22.0 ± 0.07 °C, a pH of 7.57 ± 0.26, conductivity of 1026.9 ± 367.74 microS/cm, alkalinity of 41.68 ± 1.14 mg/l $CaCO_3$, hardness of 193.86 ± 75.0 mg/l $CaCO_3$, and a light/dark photoperiod of 16/8 hours. The dissolved oxygen content was 8.33 ± 0.22 mg/l and was maintained through aeration. Parameters were determined at time 0 and every 24 hours thereafter.
Remark	Under the test conditions it was believed that some of the terephthalic acid was converted to a salt form. Fish loading was slightly above the 1.0 g/l recommended level, but was not believed to impact the results.
Reliability	(1) reliable without restriction
Reference	Amoco Corporation (1993) A Study of the Acute Toxicity to Fish (*Leuciscus idus melanotus*) of Terephthalic Acid. Conducted by Battelle Europe; Study # BE-EA-128-91-01-F3A-3; Reference no. 21

Type:	Semistatic
Species:	Salmo gairdneri
Exposure period:	96 hours
Unit:	mg/l
Analytical monitoring:	Unknown
LC_0:	500
LC_{50}:	798 - 1640
LC_{100}:	1500
Method:	OECD Guideline 203 "Fish, Acute Toxicity Test"
Year:	1991
GLP:	Yes
Test substance:	As prescribed by 1.1 - 1.4

Remark:	Mean value 1157 mg/l
Reference:	ICI Internal Report BLS 1200/B 1991
Type:	Static
Species:	Brachydanio rerio
Exposure period:	96 hours
Unit	mg/l
Analytical monitoring:	Unknown
LC_0:	> 500
Method:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year:	1989
GLP:	Yes
Test substance:	As prescribed by 1.1 - 1.4
Remark:	Nominal concentration. Examined at a concentration of 500 mg/l in the presence of Tween 80 (0.095 ml/l). The pH value was 8.0 at the beginning of the study and 5.0 at the end of the study. At 72 hours, some of the test material had settled to the bottom. The detection limit was 19 mg/l.
Reference:	Hoechst AG (1989): Unveroeffentlichte Untersuchung (89.0573)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES (e.g. Daphnia)

Type:	static
Species/Strain:	Water flea (*Daphnia magna*)
Exposure period:	48 hours
Unit:	mg/l
Analytical monitoring:	Yes
NOEC:	600 (nominal
EC0:	600 (nominal
EC50:	>1000 (nominal)
Method:	OECD Guideline 202, Part 1 "Daphnia sp., Acute Immobilization Test"
Year:	1991
GLP:	Yes
Test Substance:	as prescribed by 1.1-1.4
Remark:	Terephthalic acid was supplied by the Amoco Corporation. Purity was 99.9%.
Result:	Water quality parameters of pH, oxygen concentration, temperature and alkalinity remained within acceptable limits throughout the study and did not differ significantly with time or increasing concentration of test material. Conductivity of the saline control group (1660 at time 0) was higher than most other groups. Conductivity increased with increasing concentration of test material (from 570 to 1230 microS/cm at time 0 for 1000 ppm). Lethality was 1/20 (5%) in the salinity control group and 1/20 in Dahpnia exposed to 1000 ppm.
Test condition:	Adult Daphnia (approx. 20/vessel) were kept in 3.5 liter vessels containing 2 liters of Elendt M 7 medium (22 °C) and were fed with algae. Daphnia were placed in reconstituted water 24 hours prior to test. New -born Daphids were collected and held for 6 hours. The study was conducted in quadruplicate using 5 new-born Daphnia (6-20 hours)/concentration in each 300 ml test vessel. The test article was diluted with purified reconstituted water to yield nominal concentrations of 0, 80, 130, 220, 350, 600 and 1000 ppm in a total volume of 200 ml. The actual concentration of the highest exposure level was 951.5 ppm at time 0, and 982 p pm at 48 hours. A group of Daphnids was also exposed to water that contained 1.57 g NaOH that was pH adjusted by adding HCl (salinity control). Vessels were not aerated. Daphnia were maintained at 22.07 ± 0.11 °C, a pH of 7.79 ± 0.06, dissolved oxygen content of 8.31 ± 0.15 mg/l, conductivity of 929.38 ± 369.64 microS/cm, alkalinity of 42.91 ± 1.55 mg/l $CaCO_3$, hardness of 232.64 ± 12.61 mg/l $CaCO_3$, and a light/dark photoperiod of 16/8 hours. The number of immobilized fleas was noted at 0, 24 and 48 hours.

Remark:	Under the test conditions it was believed that some of the terephthalic acid was converted to a salt. Immobilization at the highest dose was only noted in 1 of the 20 fleas.
Reliability:	(1) reliable without restriction
Reference:	Amoco Corporation (1993) A Study of the Acute immobilisation to Daphnia of Terephthalic Acid. Conducted by Battelle Europe; Study # BE-EA-128-91-02-DAK-3;

4.3 TOXICITY TO AQUATIC PLANTS

Type:	Static
Species:	Algae (*Scenedesmus subspicatus*)
Endpoint:	growth inhibition
Exposure period:	96 hours
Unit:	mg/l
Analytical monitoring:	Yes
Toxic Limit Conc:	no toxicity was observed
NOEC:	>1000 (nominal)
EC50:	>1000 (nominal)
Method:	OECD Guideline 201, "Alga, Growth Inhibition Test"
Year:	1991-1992
GLP:	Yes
Test substance:	as prescribed by 1.1-1.4
Remark:	Terephthalic acid was supplied by the Amoco Corporation. Purity was 99.9%.
Result:	The pH and temperature of flasks containing test material remained within acceptable limits throughout the study and did not vary with time or concentration of test material. The pH of the control medium increased from 8.2 to 10.2. There was no effect of test material on algal growth. The test was considered valid, as the concentration of control algae increased by a factor of 93.3 within 3 days (at least a factor of 16 is required).
Test condition:	The study was conducted in quadruplicate using 10^4 cells/ml per test concentration. A total of 100 ml of test solution was used. The age of the stock and pre-cultures were 13 and 4 days, respectively. Test vessels consisted of 300 ml Erlenmeyer flasks containing 100 ml of test solution and were capped with a cotton plug. Flasks were shaken at a rate of 80 oscillations/minute. Room temperature was 23 ± 1 °C, pH ranged from 8.1- 10.2, and a light/dark photoperiod of 24/0 hours was used. The quantum flux density was 120uE/sec-m^{-2}. Nominal test concentrations were 62.5, 125, 250, 500 and 1000 ppm. The actual concentration of the highest exposure level was 927.05 ppm at time 0 and 408.85 ppm at 96 hours. Lower concentrations were within 70-105% nominal levels at time 0, but less than 10 ppm after 96 hours. Growth inhibition was determined daily by counting the number of cells per volume of test solution (cell concentration).
Remark:	Under the test conditions it was believed that some of the terephthalic acid was converted to a salt. The decrease in concentration was believed to be due to adsorption of the material by the algae. Cells in all replicates treated with 125 – 1000 ppm were noted to have appeared paler than controls or those treated with 62.5 ppm between 48-72 hours.
Reliability:	(2) reliable with restrictions; Reliability was decreased due to difference between nominal and measured values at time 0 and 96 hours.
Reference:	Amoco Corporation (1993) A Study of the Toxicity to Algae (*Scenedesmus subspicatus*) of Terephthalic Acid. Conducted by Battelle Europe; Study # BE-EA-128-91-02-ALG-3; Reference

4.4 TOXICITY TO MICROORGANISMS (e.g. Bacteria)

Type:	Aquatic
Species:	Activated sludge of a predominantly domestic sewage
Exposure period:	16 days

Unit:	mg/l
Analytical monitoring:	Yes
EC_{50}:	1392.8
Method:	OECD Guideline 209 "Activated Sludge, Respiration Inhibition Test"
Year:	1991
GLP:	Yes
Test substance:	As prescribed by 1.1 - 1.4
Remark:	The respiration rate of activated sludge was not inhibited at saturated concentrations during the range finding test.
Reference:	Amoco Chemicals Co. (1992) Data cited in a letter with enclosures from Amoco Chemicals Co. to ICI Chemicals & Polymers Limited. Dated January 29, 1993.

Type:	
Species:	Other protozoa: Fasciola hepatica
Exposure period:	2 hours
Unit:	mg/l
Analytical monitoring:	Unknown
EC_0:	830
Method:	Other: unknown
Year:	
GLP:	Unknown
Test substance:	No Data
Remark:	Parameters tested were mobility and change in color.
Reference:	Kurelec, Povse, Rijavec, Japelj, Globokar, Zupet (1972): Vet. Arh. 42 (1-2), 5-11

Type:	
Species:	Other protozoa: Tetrahymena pyriformis
Exposure period:	24 hours
Unit:	mg/l
Analytical monitoring:	Unknown
EC_{50}:	800
Method:	Other: motility inhibition
Year:	
GLP:	Unknown
Test substance:	No Data
Reference:	Yoshioka, Ose, Sato (1985): Sci. Total Environ. 43, 149-157

Type:	
Species:	Other: nematode: Caenorhabditis elegans
Exposure period:	Unknown
Unit:	ug/ml
Analytical monitoring:	Unknown
EC0:	1
Method:	Other: unknown
Year:	1986
GLP:	Unknown
Test substance:	No Data
Remark:	Terephthalic acid does not affect the early embryogenesis of the soil nematode Caenorhabditis elegans, but causes severe disturbance in the growth and reproduction of larval and adult C. elegans. One ug/ml arrests the growth of L1 larvae at the L1-L2 stage. However, embryos can develop normally to hatching even in the presence of TPA.
Reference:	Tabuse, Y., Miwa, J. (1986) Dev. Growth Differ. 28(4): 410 [BIOSIS/87/05608]

4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS

4.5.1 CHRONIC TOXICITY TO FISH

Not Available

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES (e.g. Daphnia)

Not Available

4.6 TERRESTRIAL ORGANISMS

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

Not Available

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Species:	Avena sativa (Monocotyledon)
Endpoint:	Other: seedling root elongation
Expos. Period:	1 day
Unit:	mg/l
EC_0:	100
Method:	Unknown
Year:	
GLP:	Unknown
Test substance:	No data
Remark:	Nominal concentration.
Reference:	Isogai, Komoda, Okamoto (1972): Sci. Pap. Coll. Gen. Educ., Univ. Tokyo 22(2), 129-135
Species:	Oryza sativa (Monocotyledon)
Endpoint:	Other: seedling root elongation
Expos. period:	5 days
Unit:	mg/l
EC_0 :	> 10
EC_{20} :	100
Method:	Unknown
Year:	
GLP:	Unknown
Test substance:	No data
Remark:	Nominal concentration
Reference:	Isogai, Komoda, Okamoto (1972): Sci. Pap. Coll. Gen. Educ., Univ. Tokyo 22(2), 129-135

4.6.3 TOXICITY TO OTHER NON-MAMMALIAN TERRESTRIAL ORGANISMS

Species:	Drosophila melanogaster
Endpoint:	mortality
Expos. period:	3 days
Unit:	mg/kg bw
LC_0:	166
Method:	Unknown
Year:	
GLP:	Unknown
Test substance:	No data
Remark:	Larva and pupa
Reference:	Goncharova, Kuzhir, Levina (1984): Vestsi Akad. Navuk BSSR, Ser. Biyal. Navuk, 47-50
Species:	White Leghorn-Chicken
Endpoint:	
Expos. period:	
Unit:	mg/kg/day
Method:	Unknown
Year:	
GLP:	Unknown
Test substance:	No data
Remark:	No information on egg laying and Eirqualitaet.

Reference: Pepper, Slinger, Summers, McConachie (1967): Poult. Sci. 46(2), 411-417

4.7 BIOLOGICAL EFFECTS MONITORING

Not Available

4.8 BIOTRANSFORMATION AND KINETICS EXCLUDING MAMMALS

Not Available

4.9 ADDITIONAL REMARKS

None

5.0 TOXICITY

5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

Type:	LD50
Species:	rat
Strain:	Sprague-Dawley
Sex:	male and female
Number of animals:	5/sex
Vehicle:	water
Value:	> 5,000 mg/kg bw
Method:	other: limit
Year:	1990
GLP:	yes
Test substance:	as prescribed by 1.1-1.4
Remark:	Terephthalic acid was supplied by the Amoco Corporation. Purity was not noted but typically exceeds 99%.
Result:	No deaths were noted in either sex. Clinical signs consisted of diarrhea (M 5/5; F 5/5), redness around nose (M 3/5; F 2/5), and discolored inguinal fur (M 4/5; F 1/5). Signs diminished in most animals by 48 hours and all were normal at study termination. Mean body weights increased during the study. No alterations were noted during gross necropsy.
Test condition:	A single dose of 5000 mg/kg test material (diluted with water to form a 50% w/v suspension) was administered by oral gavage at a rate of 10 ml/kg. At initiation of dosing rats were approximately 9 weeks of age and weighed an average of 310 g (M) and 183 g (F). Body weights were assessed at dosing, and on Days 7 and 14. Animals were observed daily for 14 days at which time they were killed and necropsied.
Reliability:	(1) reliable without restriction
Reference:	Amoco Corporation (1990) Acute Oral Toxicity Study of Terephthalic Acid in Rats. Conducted by IIT Research Institute. IITRI Study #1557

Type:	LD_{50}
Species:	Rat
Value:	> 15380 mg/kg
Method:	Other
Year:	1975
GLP:	No
Test substance:	As prescribed by 1.1 - 1.4
Remark:	
Reference:	Amoco Corporation (1975) Acute Oral Toxicity Study With Terephthalic Acid in Rats. Conducted by Industrial Bio Test Laboratories, Inc. IBT Study #601-06339

Type:	LD_{50}
Species:	Rat
Value:	1960 mg/kg
Method:	
Year:	1966
GLP:	Unknown
Test substance:	As prescribed by 1.1 - 1.4
Reference:	Caujolle et al. (1991) Comptes Rendus 160, 1079-1100 1966

Type:	LD_{50}
Species:	Rat
Value:	18800 mg/kg
Method:	
Year:	1972

GLP: Unknown
Test substance: As prescribed by 1.1 - 1.4
Reference: Marhold. (1972) Sbornik Vysledku Toxicologickeho Vysentreni Latek a Pripavku 1971: 52

Type: LD_{50}
Species: Rat
Value: >5000 mg/kg
Method:
Year: 1966
GLP: Unknown
Test substance: As prescribed by 1.1 - 1.4
Reference: Massman. (1966) Inst Fuer Arbeitsmedizin der Uni Tuebingen, 1966

Type: LD_{50}
Species: Mouse
Value: >5000 mg/kg
Method:
Year: 1968
GLP: Unknown
Test substance: As prescribed by 1.1 - 1.4
Remark:
Reference: Hoshi A, Yanai R, Kuretani K. (1968) Toxicity of terephthalic acid Chem Pharm Bull 16 1655-1660

Type: LD_{50}
Species: Mouse
Value: 6400 mg/kg
Method:
Year: Unknown
GLP: Unknown
Test substance: As prescribed by 1.1 - 1.4
Reference: Moffitt AE, Clary JJ, Lewis TR, Blanck MD, Perone VB. (1975) Absorption, distribution, and excretion of terephthalic acid and dimethyl terephthalate. Amer Ind Hyg Assoc J 36, 633-641

Type: LD_{50}
Species: Mouse
Value: 1470 mg/kg
Method:
Year: 1966
GLP: Unknown
Test substance: As prescribed by 1.1 - 1.4
Reference: Moffitt AE, Clary JJ, Lewis TR, Blanck MD, Perone VB. (1975) Absorption, distribution, and excretion of terephthalic acid and dimethyl terephthalate. Amer Ind Hyg Assoc J 36, 633-641

Type: LD_{0}
Species: Rat
Value: 2000 mg/kg
Method:
Year: 1947
GLP: Unknown
Test substance: As prescribed by 1.1 - 1.4
Reference: DuPont unpublished study, MR 170-042

Type: Other
Species: Mouse
Value:
Method:
Year: 1965
GLP: Unknown
Test substance: No data

Remark:	At 10 gm/kg (in 5% in starch): distributed movement co-ordination, damaged gastrointestinal tract, caused fluid retention, and tissue death in internal organs. 40% of treated animals died within 6-12 days. At 5 gm/kg: pronounced "vascular" disorders, effects on nervous system function and a reduced rate. At 0.5 gm/kg: only mild transient effects on the nervous system - excitation and depression.
Reference:	Moffitt AE, Clary JJ, Lewis TR, Blanck MD, Perone VB. (1975) Absorption, distribution, and excretion of terephthalic acid and dimethyl terephthalate. Amer Ind Hyg Assoc J 36, 633-641

5.1.2 ACUTE INHALATION TOXICITY

Type:	LC50
Species:	rat
Strain:	Sprague-Dawley
Sex:	male and female
Number of animals:	5/sex
Vehicle:	NA
Exposure time:	2 hours
Value:	> 2.02 mg/l
Method:	other: limit
Year:	1987
GLP:	yes
Test substance:	as prescribed by 1.1-1.4
Remark:	Terephthalic acid was supplied by the Amoco Corporation. Purity was not noted but typically exceeds 99%.
Result:	No deaths were noted in either sex. Clinical signs consisted of: normal (M 1/5; F 3/5); diarrhea (M :3/5); redness around nose (M 4/5; F 1/5); wet inguinal fur (F 1/5); discolored inguinal fur (M 3/5; F 2/5); discolored abdominal fur (F 1/5); and abdominal hair loss (F 1/5). Mean body weights increased during the study. Alterations noted during gross necropsy consisted of: normal (M 3/5; F 4/5); dark lungs (M 1/5); and enlarged mandibular lymph node (M 1/5; F 1/5).
Test condition	Animals were exposed to a single 2.02 mg/l concentration of test material as a particulate aerosol for two hours. A time-weighted average concentration was determined by gravimetric analysis. Exposure occurred in 68.2 L glass chambers at a temperature of 21 ^{o}C and relative humidity of 40%. At initiation of exposure rats weighed an average of 198 g (M) and 167 g (F). Body weights were assessed at time of exposure and on Days 7 and 14. Animals were rinsed in warm water after exposure to remove test material from skin. Animals were observed daily for 14 days at which time they were killed and necropsied.
Remark:	Technical difficulties prevented sizing of the particulate test material and the protocol-desired exposure concentration of 5 mg/l for 4 hours. Thus, animals underwent only a 2 hour exposure to 2.02 mg/l.
Reliability:	(2) reliable with restrictions; Reliability was decreased due to inability to measure test particle size.
Reference:	Amoco Chemicals Corporation (1987) Acute Inhalation Toxicity Study of Purified Terephthalic Acid in Rats. Conducted by IIT Research Institute. IITRI Study #1158;

Type:	Other
Species:	Rat
Exposure time:	4 hour
Value:	
Method:	Other
Year:	1987
GLP:	Yes
Test substance:	As prescribed by 1.1 - 1
Remarks:	Groups of 10 male rats were each exposed nose only for a single four hour period to aerosols of terephthalic acid at target concentrations of 30, 100 or 1000 mg/m^3. No t reatment related abnormalities were observed.
Reference:	ICI Internal Report CTL/R/919 (1987)

Type:	Other
Species:	Mouse
Exposure time:	10 minutes
Value:	1 mg/l
Method:	Other
Year:	1987
GLP:	Yes
Test substance:	As prescribed by 1.1 - 1.4
Remark:	Groups of 5 male mice were each exposed, nose only, for a single 10 minute period to aerosols of terephthalic acid at target concentrations of 1000 mg/m^3. Their respiratory rate was measured using optical plethysmography, before, during and after exposure. A mean rate of depression of 19% was measured indicating that terephthalic acid has a low irritant potential.
Reference:	ICI Internal Report CTL/R/919 (1987)

5.1.3 ACUTE DERMAL TOXICITY

Type:	LD_{50}
Species:	Rabbit
Strain:	New Zealand
Sex:	male and female
Number of animals:	5/sex
Vehicle:	None
Value:	> 2000 mg/kg bw
Method:	other: limit dose
Year:	1990
GLP:	Yes
Test substance:	as prescribed by 1.1-1.4
Remark:	Terephthalic acid was supplied by the Amoco Corporation. Purity was not noted but typically exceeds 99%.
Result:	No deaths were noted in either sex. The only clinical signs noted consisted of an erythema at the application site immediately after unwrapping in 2/5 males and 4/5 females. All animals appeared normal by Day 4. Mean body weights increased during the study. No alterations were noted during gross necropsy.
Test condition:	At initiation of exposure rabbits were about 3 months of age and weighed an average of 2.59 kg (M) and 2.45 kg (F). Prior to application, the backs were shaved and moistened with water. A single dose of 2000 mg/kg test material (a neat powder) was applied on the back and covered with an occlusive wrap. Body weights were assessed at dosing, and on Days 7 and 14. Animals were observed daily for 14 days at which time they were killed and necropsied.
Reliability:	(1) reliable without restriction
Reference	Amoco Chemicals Co. (1990) Acute Dermal Toxicity Study of Terephthalic Acid in Rabbits. Test Study Reference: IITRI SN 1558, TA# 445F;

5.1.4 ACUTE TOXICITY BY OTHER ROUTES OF EXPOSURE

Type:	LD_{50}
Species:	Rat
Route of admin.:	i.p.
Value:	2250 mg/kg
Method:	
Year:	1966
GLP:	Unknown
Test substance:	
Reference:	Massman. (1966) Inst Fuer Arbeitsmedizin der Uni Tuebingen, 1966

Type:	LD_{50}
Species:	Rat

Route of admin.: i.p.
Value: 1210 mg/kg
Method:
Year: 1966
GLP: Unknown
Test substance: No data
Reference: Caujolle et al. (1991) Comptes Rendus 160, 1079-1100 1966

Type: LD_{50}
Species: Mouse
Route of admin.: i.p.
Value: 880 mg/kg
Method:
Year: 1966
GLP: Unknown
Test substance: No data
Reference: Caujolle et al. (1991) Comptes Rendus 160, 1079-1100 1966

Type: LD_{50}
Species: Mouse
Route of admin.: i.p.
Value: 1430 mg/kg
Method:
Year: 1968
GLP: Unknown
Test substance: No data
Reference: Hoshi A, Yanai R, Kuretani K. (1968) Toxicity of terephthalic acid Chem Pharm Bull 16 1655-1660

Type: LD_{50}
Species: Mouse
Route of admin.: i.p.
Value: 1900 mg/kg
Method:
Year:
GLP: Unknown
Test substance: No data
Reference: Grigas EO, Ruiz R, Ariado DM. (1971) Cardiopulmonary effects of antimalarial drugs IV terephthalic acid and its dihydroxamic derivative. Toxicol Appl Pharmacol 18, 469-486

Type: LD_{50}
Species: Mouse
Route of admin.: i.v.
Value: 770 mg/kg
Method:
Year: 1966
GLP: Unknown
Test substance: No data
Reference: Caujolle et al. (1991) Comptes Rendus 160, 1079-1100 1966

Type: LD_{100}
Species: Dog
Route of admin.: i.v.
Value: 767 mg/kg
Method:
Year: 1971
GLP: Unknown
Test substance: No data
Reference: Grigas EO, Ruiz R, Ariado DM. (1971) Cardiopulmonary effects of antimalarial drugs IV terephthalic acid and its dihydroxamic derivative. Toxicol Appl Pharmacol 18, 469-486

Type:	LD_0
Species:	Mice, rats, rabbits, cats, dogs
Route of admin:	i.v.
Value:	100 - 700 mg/kg
Method:	Unknown
Year:	1971
GLP:	Unknown
Test substance:	No data
Remark:	The pharmacological features of terephthalic acid were examined in mice, rats, rabbits, cats, and dogs. The injection of sublethal amounts of terephthalic acid progressively stimulated respiration, increased pulmonary resistance, and decreased pulmonary compliance. Dogs were given 100 to 700 mg/kg of terephthalic acid intravenously. After 100 mg/kg, the respiratory minute volume was elevated; after 500 mg/kg, pulmonary compliance was decreased; and after 600 mg/kg, a decreased in aortic blood pressure occurred. Death of the dogs was preceded by respiratory arrest and an abrupt decrease in aortic blood pressure.
Reference:	Grigas EO, Ruiz R, Ariado DM. (1971) Cardiopulmonary effects of antimalarial drugs IV terephthalic acid and its dihydroxamic derivative. Toxicol Appl Pharmacol 18, 469-486.

5.2 CORROSIVENESS AND IRRITATION

5.2.1 SKIN IRRITATION

Species:	Rabbit
Result:	Not irritating
EC classificat.:	Not irritating
Method:	
Year:	1990
GLP:	Yes
Test substance:	As prescribed by 1.1 - 1.4
Remark:	No irritancy or corrosivity was observed.
Reference:	Amoco Corporation (1990) Abbreviated Acute Dermal Irritancy / Corrosivity Study of Terephthalic Acid in Rabbits. Conducted by IIT Research Institute. IITRI Study #1556.

Species:	Rabbit
Result:	Slightly irritating
EC classificat.:	Not irritating
Method:	
Year:	1975
GLP:	No
Test substance :	No data
Reference:	Amoco Corporation (1975) Primary Skin Irritation Test with Terephthalic Acid in Rabbits. IBT Study #601-06339.

5.2.2 EYE IRRITATION

Species:	Rabbit
Result:	Not irritating
EC classificat.:	Not irritating
Method:	Other
Year:	1990
GLP:	Yes
Test substance:	As prescribed by 1.1 - 1.4
Remark:	Virtually no irritation was observed.
Reference:	Amoco Corporation (1990) Abbreviated Primary Eye Irritation Study of Terephthalic Acid in Rabbits. Conducted by IIT Research Institute. IITRI Study #1555.

Species:	Rabbit
Result:	Slightly irritating
EC classificat.:	Not irritating
Method:	Other
Year:	1975
GLP:	No
Test substance:	No data
Reference:	Amoco Corporation (1975) Eye Irritation Test with Terephthalic Acid in Rabbits. IBT Study #601-06339.

Species:	Rabbit
Result:	Slightly irritating
EC classificat.:	
Method:	
Year:	Unknown
GLP:	Unknown
Test substance:	No data
Reference:	Moffitt AE, Clary JJ, Lewis TR, Blanck MD, Perone VB. (1975) Absorption, distribution, and excretion of terephthalic acid and dimethyl terephthalate. Amer Ind Hyg Assoc J 36, 633-641

Species:	Rabbit
Result:	Slightly irritating
EC classificat.:	
Method:	
Year:	1986
GLP:	Unknown
Test substance:	No data
Reference:	Prehled Prumyslove Toxikol Org Latky 317, 1986, Cited in RTECS.

5.3 SENSITIZATION

Type:	Guinea pig
Species:	
Result:	Not sensitizing
Classification:	
Method:	
Year:	Unknown
GLP:	Unknown
Test substance:	No data
Remark:	
Reference:	Moffitt AE, Clary JJ, Lewis TR, Blanck MD, Perone VB. (1975) Absorption, distribution, and excretion of terephthalic acid and dimethyl terephthalate. Amer Ind Hyg Assoc J 36, 633-641

5.4 REPEATED DOSE TOXICITY

Species:	Rat
Sex:	male and female
Strain:	other: Albino
Route of admin.:	oral feed
Exposure period:	15 weeks
Frequency of treatment:	daily in diet
Post obs. period:	None
Doses:	0.05, 0.16, 0.50, 1.6, and 5.0%
Control group:	yes, concurrent no treatment
NOAEL:	1.6% (approximately 1220 mg/kg in males and 1456 mg/kg in females)
LOAEL:	5.0% (approximately 3837 mg/kg in males and 4523 mg/kg in females)
Method:	other
Year:	1970

GLP:	no (pre-GLP)
Test substance:	as prescribed by 1.1-1.4
Remark:	Terephthalic acid was supplied by the Amoco Chemicals Corporation. Purity was not noted but typically exceeds 99%.
Result:	Survival: 4 animals (one male at 0.5% (Day 56) and three females in the highest dose (Days 54, 87, and 90) died of unknown etiology. Clinical signs: Hematuria was noted on a sporadic basis in the latter two thirds of the study in males treated with 5.0%. Growth: Body weights from both sexes treated with 5.0% were mildly depressed. Food Intake: No effects were noted. Hematology : No effects were noted. Clinical Chemistry : No effects were noted. Urinalysis: The only noteworthy finding was evidence of occult blood. Positive values were sporadically observed in males of all dose groups (except the lowest level) and in females at all treatment levels (number of animals affected was not listed). Occult blood was noted primarily at the 3 month examination time point except in the high dose animals of both sexes which showed evidence at 30, 60, and 90 days. It was usually noted as "small". Gross Pathology : Findings of interest were limited to the urinary bladder. Calculi were noted in males treated with 5% (3/3 at 30 days, 2/3 at 60 days, 2/3 at 90 days, and 9/17 at 105 days). Organ Weights: No differences were noted that were deemed attributable to exposure to test material. Microscopic Pathology : Proliferative changes (hyperplasia) were noted in the urinary bladder and occasionally the kidney pelvis epithelium of all test groups and controls. These changes were significantly increased in both their incidence and severity in high dose (5%) males. This observation was deemed inconclusive in high dose females.
Remark:	The hyperplastic change noted in the bladder is believed to be secondary to the chronic irritation induced by the presence of calculi. The bladder calculi and subsequent inflammation and hyperplasia seem to be threshold effects in that only animals in the high dose group (5%) displayed this pattern of pathology.
Test condition:	Animals (66-79 gram range) were divided into 7 groups of 60 each (30/sex) that corresponded to 2 control groups and 5 test groups (0.05, 0.16, 0.50, 1.6 and 5.0% test material in diet). Food and water were supplied *ad libitum*. Parameters assessed included: survival, clinical observations, growth, food consumption, hematology, serum clinical chemistries, urinalysis, gross pathology, and weights and histology of a full range of organs. Sacrifices were completed on 6 rats (3/sex) on Days 30, 60, and 90. All remaining animals were terminated on Day 105. Data were analyzed using analysis of variance and Duncan multiple range tests.
Remark:	The NOAEL listed is for the critical effect (bladder calculi and subsequent hyperplasia). Doses of 0.05%, 0.16%, 0.5%, 1.6% and 5% corresponded to approximately 37.9, 122, 393, 1220 and 3837 mg/kg in males and 46, 147, 447, 1456 and 4523 mg/kg in females, respectively (based on average body weight and food intake).
Reliability:	(2) reliable with restrictions; Reliability was decreased due to age of study and lack of test article purity.
Reference:	Amoco Corporation (1970). Fifteen Week Oral Toxicity of Terephthalic Acid – Albino Rats. Conducted by Toxicological Evaluations. LSL Study#1358
Species:	Rat
Sex:	Male
Strain:	
Route of admin.:	Inhalation
Exposure period:	28 days
Frequency of treatment:	6 hours per day, 5 days per week for 4 weeks
Post. obs. period:	
Doses:	21.5 mg/m^3

Control Group:	
NOAEL:	21.5 mg/m^3
Method:	Other
Year:	1973
GLP:	No
Test substance:	As prescribed in 1.1 - 1.4
Result:	No deaths were recorded and no signs of toxicity or gross pathological changes were noted. No histopathology was conducted.
Reference:	Amoco Corporation (1973) Four Week Inhalation Toxicity Assessment of Terephthalic Acid in Albino Rats. Conducted by Food and Drug Research Laboratories, Inc. FDRL Study #1610
Species:	Rat
Sex:	Male/female
Strain:	
Route of admin.:	Inhalation
Exposure period:	28 days
Frequency of treatment:	6 hours per day for 4 weeks
Post. obs. period:	3 days
Doses:	0, 0.52, 1.2, 3.3 mg/m^3
Control Group:	Yes, concurrent no treatment
NOAEL:	
Method:	
Year:	1987
GLP:	Yes
Test substance:	As prescribed in 1.1 - 1.4
Result:	No deaths occurred in the study. No differences were observed in clinical chemistry, hematology, body or organ weight changes. Histopathological findings consisted of minimal tracheal epithelial lining degeneration observed in 19/20 high-exposure rats, compared to 1/20 in control rats. There were no differences in any measured physiological parameters between control and high-exposure groups. In follow-up work, the incidence of minimal degeneration changes in the epithelial lining of the trachea was 5%, 30%, 65%, and 95% at exposures of 0, 0.52, 1.2, and 3.3 mg/m^3, respectively.
Reference:	(1) Amoco Corporation (1973) 4-Week Inhalation Toxicity Study of Terephthalic Acid (TA) In Rats. Conducted by IIT Research Institute. IITRI Study #1104 (2) Jernigan JD, Leach CL, Hatoum NS, Talsma DM, Garvin PJ. (1988) Four-week inhalation study of terephthalic acid. Toxicologist 8(1), 1005
Species:	Rat
Sex:	Male
Strain:	Sprague-Dawley
Route of admin.:	Inhalation
Exposure period:	6 months
Frequency of treatment:	6 hr/day, 5 days/week
Post. obs. period:	
Doses:	10 mg/m^3
Control Group:	Yes, concurrent no treatment
Method:	
Year:	1982
GLP:	Unknown
Test substance:	As prescribed in 1.1 - 1.4
Remark:	10 mg/m^3 - "respirable" dust conc. = 5 mg/m^3. No effects on body weights, organ (lung, liver, kidney, spleen) weights, clinical chemistry or tissue structure.
Reference:	(1) Heck HD, Tyl RW (1985) The induction of bladder stones by terephthalic acid, dimethyl terephthalate, and melamine 2,4,6-triamino-s-triazine) and its relevance to risk assessment. Regul Toxicol Pharmacol 5(3), 294-313

	(2) Lewis TR, Lynch DW, Schules RL. (1982) Absence of urinary bladder and kidney toxicity in rats and guinea pigs exposed to inhaled terephthalic acid and dimethyl terephthalate Toxicologist 2 25
Species:	Guinea pig
Sex:	Male
Strain:	Hartley
Route of admin.:	Inhalation
Exposure period:	6 months
Frequency of treatment:	6 hr/day, 5 days/week
Post. obs. period:	
Doses:	10 mg/m^3
Control Group:	Yes, concurrent no treatment
Method:	
Year:	1982
GLP:	Unknown
Test substance:	No data
Remark:	10 mg/m^3 - "respirable" dust conc. = 5 mg/m^3. No effects on body weights, organ (lung, liver, kidney, spleen) weights, clinical chemistry or tissue structure.
Reference:	(1) Heck HD, Tyl RW (1985) The induction of bladder stones by terephthalic acid, dimethyl terephthalate, and melamine 2,4,6-triamino-s-triazine) and its relevance to risk assessment. Regul Toxicol Pharmacol 5(3), 294-313 (2) Lewis TR, Lynch DW, Schules RL. (1982) Absence of urinary bladder and kidney toxicity in rats and guinea pigs exposed to inhaled terephthalic acid and dimethyl terephthalate Toxicologist 2 25
Species:	Rat
Sex:	Unknown
Strain:	
Route of admin.:	Inhalation
Exposure period:	
Frequency of treatment:	
Post. obs. period:	
Doses:	
Control Group:	Unknown
Method:	
Year:	1984
GLP:	Unknown
Test substance:	No data
Remark:	"Chronic" exposure to 0.08 mg/m^3 terephthalic acid decreased the intensity of noradrenaline uptake. At 0.4 mg/m^3, the uptake was decreased by 25%. At 1 mg/m^3, the uptake decrease was 62%. Exposure to 0.08 and 0.4 mg/m^3 caused some increase in monoamine oxidase of the cerebral hemisphere, and at 1 mg/m^3 increased enzyme was 26%. Catecholamine o-methyltransferase activity also increased in the cerebral hemisphere at 0.4 mg/m^3, being higher at 1 mg/m^3. Reported to presumably affect the catecholamine inactivation mechanism of the CNS.
Reference:	Davidenko AV, Vasil ev AN, Kucherenko-N-E. (1984) (Functioning of the systems of neuromediator inactivation in the brain terminals of rats chronically exposed to terephthalic acid and its dimethyl ester). Biol Nauki ISS 1 31-4
Species:	Rat
Sex:	Male/female
Strain:	Wistar
Route of admin.:	Oral feed
Exposure period:	90 days
Frequency of treatment:	Continuous

Post. obs. period:	
Doses:	3.0% in the diet
Control Group:	Yes, concurrent no treatment
Method:	Other
Year:	1975
GLP:	No
Test substance:	As prescribed by 1.1 - 1.4
Remark:	Animals were fed 5% terephthalic acid in the diet for 1 weeks, which was then reduced to 3% for the remainder of the study. Pathological effects were limited to the kidney and bladder. Terephthalic acid induced bladder stones in 11/18 males and 3/19 females. Mild to moderate hyperplasia of the bladder urothelium was diagnosed in 13/18 males and 3/19 females. A strong correlation was found between the presence of uroliths and the development of bladder hyperplasia: 62% of the TPA males (8/13) and 100% of the TPA females (3/3) diagnosed as having transitional cell hyperplasia also had bladder stones. It is possible that microscopic calculi were passed or were lost during sectioning of bladder tissue for histopathology. This could explain the failure to detect uroliths in all of the hyperplastic bladders.
Reference:	Amoco Corporation (1972) Subacute Feeding Studies (13 Week) In Rats with Dimethylterephthalate (DMT), Isophthalic Acid (IA) and Terephthalic Acid (TA). Conducted by Food and Drug Research Laboratories. FDRL Study #0411
Species:	Weanling rat
Sex:	Male/female
Strain:	Fischer 344
Route of admin.:	Oral feed
Exposure period:	2 weeks
Frequency of treatment:	Daily
Post. obs. period:	
Doses:	0.5, 1.5, 3.0, 4.0, or 5.0%
Control Group:	Yes, concurrent no treatment
NOAEL:	
Method:	
Year:	1981
GLP:	Unknown
Test substance:	As prescribed in 1.1 - 1.4
Remark:	Exposure resulted in a 93.3% incidence of bladder calculi in male pups receiving 5% dietary terephthalic acid (TPA). Female pups also developed stones, but at a lower frequency. The dose-response curves for stone induction were extremely steep: no stones were induced at dietary concentrations below 1.5%. Histological examination of the urinary tract revealed extensive hyperplasia of the transitional epithelium only in the urinary bladders that contained calculi. Analysis of calculi indicated a heterogeneous chemical composition. The principal components (by weight) were: TPA, calcium, phosphate, and protein in the TPA -induced stones. Concentrations of calcium, TPA, and phosphate, as well as pH, were determined in the urine of weanling rats at study termination. TPA induced urinary acidosis and hypercalciuria in the range of doses used. Results indicate that critical saturating urinary concentrations of TPA and calcium are necessary for stones to develop following TPA exposure, and that calculus formation appears to be a prerequisite for the induction of TPA-induced bladder hyperplasia.
Reference:	(1) Chin TY, Tyl RW, Popp JA, Heck HD. (1981) Chemical urolithiasis. 1. Characteristics of bladder stone induction by terephthalic acid and dimethyl terephthalate in weanling Fischer-344 rats. Toxicol Appl Pharmacol 58(2), 307-21 (2) CIIT (1982) A Ninety-Day Study of Terephthalic Acid (CAS No. 100-21-0) Induced Urolithiasis and Reproduction Performance in Wistar and CD Rats. CITI Docket 11622
Species:	Rat

Sex:	Male/female
Strain:	Wistar
Route of admin.:	Oral feed
Exposure period:	2 yr
Frequency of treatment:	Daily
Post. obs. period:	
Doses:	20, 142, 1000 mg/kg/day
Control Group:	Yes, concurrent no treatment
Method:	
Year:	1983
GLP:	Unknown
Test substance:	As prescribed in 1.1 - 1.4
Remark:	Terephthalic acid induced bladder stones were seen in 13/126 females in the high dose group. At the scheduled 6 and 12 month sacrifices, no bladder calculi were detected. At the 18 month sacrifice sand like particle or bladder calculi were only seen in two of the high dose females. The high-dose corresponds to an approximate dietary concentration of 2.0 to 2.8% in adult F-344 rats.
Reference:	CIIT (1983) Chronic Dietary Administration Of Terephthalic Acid. CIIT Docket 20124

Species:	Rat
Sex:	Male
Strain:	
Route of admin.:	Oral feed
Exposure period:	14 days
Frequency of treatment:	Daily
Post. obs. period:	
Doses:	4%
Control Group:	Yes, concurrent no treatment
Method:	
Year:	1983
GLP:	Unknown
Test substance:	As prescribed in 1.1 - 1.4
Remark:	Terephthalic acid-induced urolithiasis in male weanling rats was abolished by therapeutic agents which reduced urinary calcium and terephthalic acid (TPA) excretion (chlorothiazole), or which enhanced water intake, urinary magnesium and TPA excretion, and ameliorated TPA-induced aciduria (dietary bicarbonate).
Reference:	Wolkowski-Tyl R, Chin TY (1982) Effects of selected therapeutic agents on urolithiasis induced by terephthalic acid in the male weanling Fischer 344 rat. Fundam Appl Toxicol 3(6), 552-8

Species:	Rat
Sex:	Unknown
Strain:	Unknown
Route of admin.:	Oral feed
Exposure period:	90 days
Frequency of treatment:	Daily
Post. obs. period:	
Doses:	0, 1, 3.2, or 10%
Control Group:	Yes, concurrent no treatment
Method:	
Year:	1955
GLP:	Unknown
Test substance:	As prescribed in 1.1 - 1.4
Remark:	At the 1 and 3.2% levels, all rats survived, and there were no effects on growth or adverse clinical signs of toxicity. Hematology was normal. In the 1% group, there were no adverse histopathological effects. However, 2/12 animals in the 3% group showed effects on the urinary tract due to calculi. In the 10% group, 8/12 animals survived, and there was marked retardation of growth. Hematuria and urinary calculi were severe.

	Addition of 5% sodium bicarbonate to the diet of the 10% group modified but did not completely nullify the effects of terephthalic acid.
Reference:	DuPont unpublished study, MR 281-001
Species:	Rat
Sex:	Female
Strain:	
Route of admin.:	i.p.
Exposure period:	102 days
Frequency of treatment:	Every 7 days
Post. obs. period:	
Doses:	0.3 - 0.6 ml/animal (15% suspension olive oil)
Control Group:	Unknown specified
Method:	
Year:	1966
GLP:	Unknown
Test substance:	No data
Remark:	After 6 weeks, reduced body weight. No adverse toxic effect or pathological findings observed.
Reference:	Massman. (1966) Inst Fuer Arbeitsmedizin der Uni Tuebingen, 1966
Species:	Mouse
Sex:	Female
Strain:	Swiss
Route of admin.:	Oral feed
Exposure period:	7 days
Frequency of treatment:	Daily
Post. obs. period:	
Doses:	0.5%
Control Group:	Yes, concurrent no treatment
Method:	
Year:	1968
GLP:	Unknown
Test substance:	No data
Remark:	No effect on phenolsulfophthalein (PSP) dye excretion from kidney, the transaminase activity (GOT and GPT) in blood plasma, and the contents of sugar, protein, free amino acids, and urea in blood plasma. The BSP retention in the liver was not increased, but rather decreased. The barbiturate sleeping-time was shortened markedly by terephthalic acid feeding.
Reference:	Hoshi A, Yanai R, Kuretani K. (1968) Toxicity of terephthalic acid Chem Pharm Bull 16 1655-1660
Species:	Rat
Sex:	Unknown
Strain:	Sprague-Dawley
Route of admin.:	
Exposure period:	
Frequency of treatment:	Unknown
Post. obs.period:	
Doses:	20 mg/kg/day
Control Group:	Unknown
Method:	
Year:	1993
GLP:	Unknown
Test substance:	No data
Remark:	Lowered serum cholesterol and triglyceride levels.
Reference:	Hall IH, Wong OT, Reynolds DJ, Simlot R, Chang JJ. (1993) Terephthalic acid in Sprague-Dawley rats as a hypolipidemic agent. Arch Pharm Weinheim 326(1), 5-13
Species:	Chicken
Sex:	Unknown

Strain:	
Route of admin.:	Oral feed
Exposure period:	
Frequency of treatment:	Unknown
Post. obs. period:	
Doses:	0.5% in diet
Control Group:	Unknown
Method:	
Year:	1965
GLP:	Unknown
Test substance:	No data
Remark:	Reduced body weight, inhibited sperm formation, induced testes damage, and effects on the pituitary and thyroid.
Reference:	Kona K, Nakajima E. (1965) Effect of terephthalic acid on the vicera of chickens II. Testis, thyroid gland and auterior lobe of pituitory. Jap Poultry Sci 2(3). 205-209

Species:	Rat
Sex:	Unknown
Strain:	Unknown
Route of Admin.:	Inhalation
Exposure period:	Daily
Frequency of treatment:	14 to 20 daily exposures
Post obs. period:	
Doses:	2 - 5 mg/m^3
Control Group:	Unknown
Method:	Unknown
Year:	1965
GLP:	Unknown
Test substance:	No data
Remark:	Exposure to atmospheres containing 2 to 5 mg/m^3 produced skin redness. Skin erosions induced by 14 to 20 daily exposures. Mucous membrane redness and increased in respiration rate was recorded. There were effects on the vascular, respiratory, and nervous systems.
Reference:	Sanina YP. (1965) The toxicity of terephthalic acid Toksikol Nov Prom Khum Vesh 7 91-101 [Chem Abstr 63, 7549 1965]

Species:	Rat
Sex:	Unknown
Strain:	Unknown
Route of admin.:	Subcutaneous
Exposure period:	10 days
Frequency of treatment:	Daily
Post. obs.period:	
Doses:	2000 mg/kg
Control Group:	Unknown
Method:	
Year:	Unknown
GLP:	Unknown
Test substance:	As prescribed in 1.1 to 1.4
Remark:	Two rats were given 2000 mg/kg terephthalic acid suspended in 1% gum acacia daily for ten days by subcutaneous injection. This dosage required three injections per day of approximately 2 ml each. The animals failed to gain weight normally but were healthy and active throughout the test. No calculi were formed.
Reference:	DuPont unpublished study, MR 281-1

5.5 GENETIC TOXICITY IN VITRO

Type:	Ames test
System of testing:	Salmonella typhimurium TA 98, TA 100, TA 1535, and TA 15375
Concentration:	0, 100, 333, 1000, 3333, 10000 µg/plate

Cytotoxic conc.:	> 10000 µg/plate
Metabolic activation:	with and without
Result:	negative in all strains with or without activation
Method:	other
Year:	1982
GLP:	no data
Test substance:	as prescribed by 1.1-1.4
Remark:	Test material was supplied by the Eastman Chemical Company. Purity was 98%.
Test condition:	Approximately 10^8 bacteria/strain were mixed with 0.5 ml of either sodium phosphate buffer (pH 7.4) or S9 mix, and test material. The metabolic activation system consisted of S9 supernatant fractions obtained from rat and hamster liver previously induced with Aroclor 1254. Test material was dissolved in DMSO solvent, incubated at 37 °C for 20 minutes, and mixed with 3 ml of molten top agar containing a trace amount of biotin and a growth-limiting amount of histidine. The mixture was then poured onto minimal agar plates and incubated at 37 °C for 48 hours, after which time histidine-revertant colonies were counted. All tests were repeated at least once. Positive controls consisted of sodium azide (TA 100, TA 1535), 4-nitro-o-phenylenediamine (TA 98), 9-aminoacridine TA 1537), and 2-aminoanthracene (all strains when using metabolic activation).
Remark:	The study was noted to have been conducted at SRI International. It was noted in the published manuscript "All chemicals were tested, under code, in a preincubation modification of the Salmonella plate incorporation assay by Ames *et al.* 1975."
Reliability:	(2) reliable with restrictions; Reliability was decreased due to the number of strains tested do not meet present guidelines.
Reference:	Zeiger E, Haworth S, Mortelmans K, Speck W. (1985). Mutagenicity testing of di(2-ethylhexyl)phthalate and related chemicals in Salmonella. Environmental Mutagen 7, 213-232

Type:	Ames test
System of testing:	Salmonella TA100, TA1535, TA1537, TA1538, TA98
Concentration:	333.3 microgram/plate
Metabolic activation:	With and without
Result:	Negative
Method:	other
Year:	1979
GLP:	Unknown
Test substance:	As prescribed by 1.1 - 1.4
Remark:	Precipitation at 10 mg/plate prevented retesting at higher doses.
Reference	ICI Internal Report CTL/C/1377 (1979)

Type:	Ames test
System of testing:	Salmonella TA98, TA100, TA1535, TA1538
Concentration:	
Metabolic activation:	With and without
Result:	Negative
Method:	
Year:	1989
GLP:	Unknown
Test substance:	As prescribed in 1.1 - 1.4
Reference:	Brooks AL, Seiler FA, Hanson RL, Henderson RF. (1989) In vitro genotoxicity of dyes present in colored smoke munitions. Environ Mol Mutagen 13, 304-313

Type:	Ames test
System of testing:	Salmonella TA100, TA98, TA97, TA102
Concentration:	
Metabolic activation:	With and without
Result:	Negative
Method:	
Year:	1989

GLP: Unknown
Test substance: No data
Reference: Monarca S, Rizzi R, Pasquini R, Pool BL, De-Fusco R, Biscardi D, Gervasoni M, Piatti E. (1989) Studies on genotoxic properties of precursors of polyethylene terephthalate plastics. Mutat Res 216, 314-315

Type: Ames test
System of testing: Salmonella TA98, TA100, TA1535, TA1537
Concentration: Up to 10 mg/plate
Metabolic activation: With and without
Result: Negative
Method:
Year: 1984
GLP: Unknown
Test substance: No data
Reference: Sarrif AM. 1984 Du Pont de Nemours & Co, Personal communication cited in Heck HD, Tyl RW. (1985) Regul Toxicol Pharmacol 5(3), 294-313

Type: Ames test
System of testing: Salmonella TA98, TA100, TA1535, TA1537
Concentration:
Metabolic activation: With and without
Result: Negative
Method:
Year: 1980
GLP: Unknown
Test substance: No data
Reference: Florin I, Rutberg L, Curvall M, Enzell CR (1980) Screening of tobacco smoke constituents for mutagenicity using the Ames' test. Toxicology 15, 219-232

Type: Cytogenetic assay
System of testing: Human peripheral blood lymphocytes
Concentration:
Metabolic activation: Unknown
Result: Negative
Method:
Year: 1989
GLP: Unknown
Test substance: No data
Reference: Monarca S, Rizzi R, Pasquini R, Pool BL, De-Fusco R, Biscardi D, Gervasoni M, Piatti E. (1989) Studies on genotoxic properties of precursors of polyethylene terephthalate plastics. Mutat Res 216, 314-315

Type:
System of testing: DNA amplification test
Concentration:
Metabolic activation: Unknown
Result: Negative
Method:
Year: 1989

GLP: Unknown
Test substance: No data
Reference: Monarca S, Rizzi R, Pasquini R, Pool BL, De-Fusco R, Biscardi D, Gervasoni M, Piatti E. (1989) Studies on genotoxic properties of precursors of polyethylene terephthalate plastics. Mutat Res 216, 314-315

Type:	
System of testing:	Chinese hamster lung fibroblasts
Concentration:	2000 ug/ml
Metabolic activation:	Without
Result:	Negative
Method:	
Year:	1988
GLP:	Unknown
Test substance:	No data
Reference:	Ishidate M, Harnois MC, Safini T. (1988) A comparative analysis of data on the clastogenicity of 951 chemical substances tested in mammalia cell cultures. Mutat Res 195, 151-213

Type:	Micronucleus assay
System of testing:	Human peripheral blood lymphocytes
Concentration:	
Metabolic activation:	Unknown
Result:	Negative
Method:	
Year:	1989
GLP:	Unknown
Test substance:	No data
Reference:	Monarca S, Rizzi R, Pasquini R, Pool BL, De-Fusco R, Biscardi D, Gervasoni M, Piatti E. (1989) Studies on genotoxic properties of precursors of polyethylene terephthalate plastics. Mutat Res 216, 314-315

Type:	Other
System of testing:	Primary rat hepatocytes
Concentration:	
Metabolic activation:	Unknown
Result:	Negative
Method:	
Year:	1989
GLP:	Unknown
Test substance:	No data
Remark:	Analysis for DNA single strand breaks.
Reference:	Monarca S, Rizzi R, Pasquini R, Pool BL, De-Fusco R, Biscardi D, Gervasoni M, Piatti E. (1989) Studies on genotoxic properties of precursors of polyethylene terephthalate plastics. Mutat Res 216, 314-315

5.6 GENETIC TOXICITY IN VIVO

Type:	Mammalian Erythrocyte Micronucleus assay
Species:	Mouse
Strain:	ICR
Sex:	male and female
Route of admin.:	single intraperitoneal (ip) injection
Exposure period:	24 and 48 hours
Method:	OECD 474
Doses:	200, 400, and 800 mg/kg
Results:	Negative
Year:	2001
GLP:	Yes
Test substance:	as prescribed by 1.1-1.4
Remark:	Terephthalic acid was supplied by the BP Amoco Chemicals Corporation. Purity was not noted but typically exceeds 99%.
Result:	Mortality was observed in 1/15 male mice that had been treated with 800 mg/kg TPA. One mouse from the replacement group was used in place of the animal that died. Clinical signs following treatment with either dose

	of TPA included lethargy and piloerection. Negative and positive control animals appeared normal during the course of the study. The total number of micronuclei observed per 20000 PCE in animals treated with vehicle, 200, 400 or 800 mg/kg for 24 hours was 4, 8, 5, and 4, respectively. The incidence of micronuclei in animals treated with 800 mg/kg also did not differ from the vehicle control at 48 hours (2/20000 vs. 8/20000, respectively). There was no difference between males and females. TPA was negative in the test. The test was valid, as the incidence of micronuclei in the vehicle control was not greater than 5/1000 PCE and the number of micronucleated cells in the positive controls (382/20000) was significantly different ($p < 0.05$) from the vehicle control. Reductions (up to 9%) in the ratio of polychromatic erythrocytes to total erythrocytes were observed in some of the treated groups relative to the vehicle control, suggesting that the test article did not inhibit erythropoiesis. Greater reductions in this ratio were observed in animals treated with cyclophosphamide (25-29%).
Test condition:	Animals were about 6-8 weeks of age at study initiation. Animals (5/sex/group) were dosed ip with vehicle (negative control), 200, 400 or 800 mg/kg TPA, or 50 mg/kg cyclophosphamide (positive control) in corn oil in a volume of 20 ml/kg body weight and were sacrificed at 24 hours. Additional animals (5/sex/group) were treated with vehicle or 800 mg/kg TPA and sacrificed at 48 hours. An additional group of 5 males and 5 females were dosed with 800 mg/kg TPA as a replacement group in case of mortality. Bone marrow samples from animals sacrificed at 24 and 48 hours were scored under oil immersion (2000 polychromat ic erythrocytes (PCE) per animal) for the presence of micronuclei. The number of micronucleated normocytes per 2000 PCE was also assessed. The proportion of PCE to total erythrocytes was also recorded on a per 1000 erythrocyte basis. Statistical significance for the incidence of micronucleated polychromatic erythrocytes was determined using Kastenbaum-Bowman Tables.
Remark:	Criteria for a valid test: The mean incidence of micronucleated polychromatic erythrocytes must not exceed 5/1000 polychromatic erythrocytes (0.5%) in the negative control vehicle. The incidence rate in the positive control group must be significantly increased relative to the negative control ($p<0.05$, Kastenbaum-Bowman Tables.
Reliability:	(1) valid without restriction
Reference:	Bioreliance. 2001. Mammalian erythrocyte micronucleus test. Study No. AA41MJ.123.BTL for BP Amoco.
Type:	Micronucleus assay
Species:	Mouse
Sex:	
Strain:	
Route of admin.:	i.p.
Exposure period:	Single (examined at 24, 48 and 72 hrs)
Doses:	0.09 - 4.30 mmol/kg
Method:	
Year:	1989
GLP:	Unknown
Test substance:	No data
Remark:	Positive: Increase in micronuclei in bone marrow polychromatic erythrocytes - peak at 24 hrs. Data from this reference were available in abstract form only. Therefore, insufficient detail existed to determine the reliability of this study. The solvent used in this study was dimethylsulfoxide (DMSO). In similar studies, use of DMSO as a vehicle resulted in excess mortality and elevated micronuclei in the negative control group. Poor study design and reporting along with solvent toxicity make interpretation of this study problematic. More detailed studies meeting current OECD protocols are available to assess the effect of terephthalic acid on this endpoint.
Reference:	Zabrejko S, Goncharova RI (1989) Clastogenic activity of some phthalates (ph) in in vivo somatic mouse cells. Mutat Res 216, 283-284

5.7 CARCINOGENICITY

Species:	Rat
Sex:	Male/female
Strain:	Fischer 344
Route of admin.:	Oral feed
Exposure period:	Lifetime (2 years)
Frequency of treatment:	Daily
Post. obs. period:	
Doses:	0, 20, 142, 1000 mg/kg/day
Control Group:	Yes, concurrent no treatment
Method:	Other
Year:	1983
GLP:	Unknown
Test substance:	As prescribed by 1.1 - 1.4
Remark:	Terephthalic acid induced bladder stones were seen in 13/126 females in the high dose group. At the scheduled 6 and 12 month sacrifices, no bladder calculi were detected. At the 18 month sacrifice sand like particle or bladder calculi were only seen in two of the high dose females. There were 19/118 females with what was described as transitional cell adenomas by one pathology laboratory and epithelial hyperplasia by another. Two of these were detected in high dose females after 18 months (2/27), 15 were seen in seen in high dose females a t the end of the study (15/79), and one was seen in a control female at the end of the study. None were found in the males, nor at any other dose level. It was believed that rats fed high concentrations of terephthalic acid in the diet develop bladder calculi which appear to cause chronic inflammation of the bladder epithelium, bladder hyperplasia and subsequently bladder tumours. An apparent threshold effect exists because animals exposed to lower concentrations for their lifetime do not form bladder calculi or tumors. The high dose group in this study (1000 mg/kg/day) corresponds to an approximate dietary concentration of 2.0% to 2.8% in adult Fisher rats.
Reference:	CIIT (1983) Chronic Dietary Administration Of Terephthalic Acid. CIIT Docket 20124

Species:	Rat
Sex:	Male/female
Strain:	Wistar
Route of admin.:	Oral feed
Exposure period:	2 years
Frequency of treatment:	Daily
Post. obs. period:	
Doses:	1% (500 mg/kg/day) & 2% (1000 mg), 5% (2500 mg)
Control Group:	Unknown
Method:	
Year:	1974
GLP:	Unknown
Test substance:	As prescribed in 1.1 - 1.4
Remark:	Reduced body weight gain occurred at in the 5% dose level (males and females) and in the 2% dose level (males). At 1%, reduced relative liver weight in females and reduced relative kidney size in males and females. At 2% , reduced liver, kidney, and heart weights (females only). At 5%, there was increased kidney weight in males, and increased adrenal weights in males and females; as well as increased mortality, mainly as a result of increased incidence of bladder stones (at 5%: males, 42/47; females, 39/42; at 1%: females, 1/48). There was increased incidence of bladder and ureter tumors (at 5%: males, 21/37; females, 21/34; at 2%: males, 1/48; females, 2/48; at 1%: males, 1/43.). There was increased incidence of bladder and ureter tumors.

Reference:	Gross J. (1974) The effects of prolonged feeding of terephthalic acid (TPA) to rats. Project FG-IS-175. Submitted to US Dept. of Agriculture, Agriculture Research Service, Washington D.C.
Species:	Mouse
Sex:	Female
Strain:	C3H
Route of admin.:	Oral feed
Exposure period:	12 months
Frequency of treatment:	Daily
Post. obs. period:	
Doses:	5%
Control Group:	Unknown
Method:	
Year:	1973
GLP:	Unknown
Test substance:	No data
Remark:	Reduced number of mammary tumours. At 12 months, mammary tumours occurred in 78% of controls and in 50% of treated mice.
Reference:	Nagasawa H, Fujimoto M. (1973) Experimentia 29, 89. Cited in BIBRA Toxicity Profile 1995

5.8 TOXICITY TO REPRODUCTION

Type:	other; one-generation
Species:	Rat
Sex:	male and female
Strain:	CD and Wistar
Route of administration:	oral; in feed
Exposure period:	paternal: 90 days prior to and throughout mating maternal: 90 days prior to mating, throughout mating, gestation, and lactation offspring: 51 days; from birth through lactation and 30 days post weaning
Frequency of treatment:	daily; in feed
Duration of test:	approximately 160 days
Doses:	0.03, 0.125, 0.5, 2.0, and 5.0%
Remark:	The approximated mg/kg doses based on average feed consumption and body weight during the 90 day pre-mating period were: CD(M): 14, 59, 240, 930, 2499 CD(F): 17, 67, 282, 1107, 2783 Wistar(M): 14, 61, 249, 960, 2480 Wistar(F): 19, 78, 307, 1219, 3018
Control group:	yes; concurrent no treatment
NOAEL Parental:	0.5% (CD; Wistar: 2.0%)
NOAEL Reproductive :	> 5.0% (CD and Wistar)
NOAEL F1 Offspring:	0.5% (CD and Wistar)
Method:	other
Year:	1982
GLP:	Yes (see remark)
Test substance:	as prescribed by 1.1-1.4
Remark:	No specific test material supplier or purity of test material was noted. A manager of quality assurance signed off on the study report. However, the report did not contain a specific statement *per se* in regard to the study being conducted under GLP assurances.
Result:	Parental Effects: Following 90 days of exposure to TPA, statistically significant decreases in food consumption were observed in CD females treated with 2% and 5%, and in both sexes of Wistars treated with 5%. Body weights were statistically decreased after 13 weeks in both sexes of CD rats on 2% and 5% TPA diets, and in males exposed to 0.03%. This effect occurred in Wistars (both sexes) only at the 5% level. There were 5 deaths (3 CD females, 1 Wistar/sex) reported during weeks 4-13 in animals given 5% TPA in the diet.

During the one-generation component of the study 3 CD (1 male at 2.0%, 1/sex at 5.0%) and 4 Wistar female (2 at 5.0% and 2 at 0.03%) rats died. There was no effect of treatment on fertility index and litter size.
Offspring Effects: There were no effects of treatment on litter size, sex ratio, or total number of offspring. While no control offspring were found dead on Day 0, 17 Wistar pups (1 at 0.03%, 2 at 0.125%, 1 at 0.5%, 12 at 2.0% (2 from one dam and 10 from another)) and 23 CD pups (1 at 0.5%, 7 at 2.0% (3 dams) and 15 at 5.0% (3 dams; with 11 from one of them)) were found dead. No statistical differences were noted in viability on Days 0, 1, or 21 in either strain. In CD rats, survivability on Day 21 was reduced in both sexes of offspring whose parents had been exposed to 5% TPA in the diet.
In Wistar rats, body weights of both sexes of offspring from dams given 5.0% were reduced at Day 1. On Day 21, body weight was reduced in both strains of offspring from dams that ingested 5% TPA in the diet. Increased postnatal deaths on Day 1 and decreased survivability to Day 21 were noted in the 2% and 5% groups. At these dose levels, several large litters of pups were lost to dams suffering obvious signs of toxicity. Several of these dams did not allow the pups to nurse or attend to the litters. These pups were noted not to have milk in their stomachs and presented clinically as being very weak. These dams were consuming dietary levels of TPA known to cause reduced feed consumption, diarrhea and gastric trichobezoars (hairballs) and induce the formation of renal and bladder calculi. Unscheduled deaths during the postweaning period (Day 21-51) were confined to the 5% TPA group (18 Wistar and 16 CD) and were associated with a very high incidence of renal and bladder calculi. Renal and bladder calculi were noted in all animals exposed to 5% that were necropsied at Day 21. Day 51 necropsy findings also reported a very high incidence of renal and bladder calculi and the histological sequelae of the presence of the calculi.

Test condition: This study contrasted the toxicity of TPA in two different strains of rats. Experimental conditions were identical for both. Rats 15-17 weeks of age (n=30) were grouped housed 3/cage for the first 90 days of exposure. Body weight and feed intake were determined weekly during this time period. On Day 91, breeding pairs (n=10/sex) were housed together for 2 weeks prior to being separated. On Day 0 (delivery) the number and viability of offspring were evaluated and grossly examined. Offspring were recounted, sexed, and weighed on Day 1. These measurements were repeated at weaning on Day 21. After weaning the litters were reduced to 2/sex/dose from each of 5 litters (20 pups/dose/strain) and maintained on test diets for 30 more days (Day 51) prior to sacrifice. There were only 9 pairs of CD strain rats at the 5% diet level. Remaining animals were necropsied within a few days post weaning. At termination offspring were grossly examined and necropsied. Parental and F1 generation animals were observed 2x/day for clinical signs. Body weight gain and standard reproductive indices were assessed and statistically compared using ANOVA and Dunnett's-t-test using SAS statistical programs. Parameters evaluated consisted of: fertility index, number of offspring born per dam; number and proportion of each sex born; number (Day 0, 1, and 21) and proportion (Day 1 and 21) of each sex alive; average weight at Day 1 and 21 of all offspring and of each sex.

Remark : Other studies have demonstrated an increased incidence of renal and bladder calculi formation in weanling animals when compared to adults consuming the same dietary level of TPA. This apparent increased sensitivity can be explained by the large amount of feed consumed in relation to body weight for young animals experiencing their initial growth spurt. Weanling animals are not more sensitive to TPA when the results are expressed on a mg/kg basis.

Conclusion: The NOAEL for reproductive toxicity was >5% in the diet (approximately 2480-3018 mg/kg/day). Whereas, the NOAEL for parental toxicity and the F1 generation was 0.5% TPA in the diet (approximately 240-307 mg/kg/day).

Reliability: (1) reliable without restriction

Reference:	CIIT (1982) A Ninety-Day Study of Terephthalic Acid (CAS No. 100-21-0) Induced Urolithiasis and Reproduction Performance in Wistar and CD Rats. CITI Docket 11622
Type:	Other
Species:	Mouse
Sex:	Male/female
Strain:	C3H
Route of admin.:	Oral feed
Exposure Period:	
Frequency of treatment:	
Duration of test:	
Doses:	
Control Group:	Unknown
Method:	
Year:	1973
GLP:	Unknown
Test substance:	No data
Remark:	Reproduction indices (interval between mating and birth of the pups, litter size, pup weights, growth rate) were normal in group of 31 females that were maintained throughout life on diet containing 0.5% (750 mg/kg/day) terephthalic acid, and allowed to produce six litters. Females were mated first after approximately 50 days treatment.
Reference:	Nagasawa H, Fujimoto M. (1973) Experimentia 29, 89. Cited in BIBRA Toxicity Profile 1995

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species:	Rat
Sex:	Female
Strain:	Sprague-Dawley
Route of admin.:	Inhalation
Exposure period:	days 6-15 of gestation
Frequency of treatment:	6 hours/day for 10 consecutive days
Duration of test:	20 days
Doses:	1.0, 5.0, and 10.0 mg/m^3
Control group:	yes; filtered room air
NOAEL Maternal:	>10.0 mg/m^3
NOAEL Fetal:	>10.0 mg/m^3
Method:	Other
Year:	1989
GLP:	Yes
Test substance:	as prescribed by 1.1-1.4
Remark:	Test material was supplied by the Amoco Corporation. Purity was not noted but typically exceeds 99%. Respirable time-weighted average concentrations were 0.90, 4.73, and 10.4 mg/m^3.
Result:	Maternal Effects: No mortalities occurred in any group. The incidences of clinical signs observed in rats exposed to TPA were similar to controls. No statistically significant differences were noted in mean dam body weight or weight gain, uterine weight, or implant number. Fetal Effects: No statistically significant differences were noted in mean litter weights, pup viability, or number of fetal malformations. External soft tissue examinations did not indicate any differences from control. However, internal examinations showed a slight increase in the incidence of rib anomalies in the middle dose (5.0 mg/m^3) group. This was only significant when all the various types of rib anomalies were added together.
Remark:	Rib anomalies were not deemed to be an indicator of teratogenesis because they were common variations, were not elevated in a dose-related manner, and occurred at a rate that was within the range of the laboratories own historical controls. Furthermore, no other signs of embryotoxicity were associated with this change.

Test condition: Female rats weighing 117-150 g were quarantined and housed 2/cage with 1 male. Confirmation of mating was via evidence of sperm in a vaginal smear (Day 0), after which females were housed singly. The study consisted of 26-27 timed-pregnant dams per dose level. Exposures were by whole body inhalation conducted in 2 m^3 chambers with an airflow rate of 305-420 l/min. Test article was ground to respirable-sized particles using a Retsch Ultra-Centrifugal Mill. Chambers were sampled 2x/exposure period and TPA levels were determined by spectrophotometric analysis. Particle size was determined using a cascade impactor. Temperature, humidity and airflow were measured hourly. Animals were observed twice daily and given detailed physical exams daily on days 0 and 6-20. Dams were weighed on Days 0, 5 (randomization into groups), 6 (exposure initiation), 11, 16, and 20 (study termination). Standard "guideline" postmortem procedures were carried out on the females and their fetuses. Data were analyzed in an appropriate statistical manner using log transformations, multivariate ANOVA, single factor ANOVA and Dunnett's-"t"-test depending on the nature and type of end-point assessed. The dam was considered to be a random factor and the pup a nested factor within the dam.

Reliability: reliable without restriction

Reference: Amoco Corporation (1989) A Segment II Inhalation Teratology Study of Terephthalic Acid in Rats. Conducted by IIT Research Institute. IITRI Study #1448; Reference no. 99

And

Ryan BM, Hatoum NS, Jernigan JD. (1990) A segment II inhalation teratology study of terephthalic acid in rats. Toxicologist 10, 40; Reference no. 100

5.10 ADDITIONAL REMARKS

Type: Pharmacokinetic study.

Remark: Sprague-Dawley rats were exposed by inhalation to a particulate aerosol of 10 mg/m^3 terephthalic acid. Exposure was 6 hours per day for 25 consecutive days, followed by a 28-day post-exposure recovery period. Blood and urine samples were collected one day prior to exposure and after 1, 5, 10, 15, 25 days of exposure and every 7 days during the 28 day recovery period. Terephthalic acid was not detected in the blood after the first 5 days of exposure. Detectable blood concentrations of terephthalic acid were observed after 10 consecutive days of exposure and progressively increased over the remaining exposure period. The highest mean blood concentration was 2.7 ug/ml after 25 days. Seven days after completion of the exposure period, the blood concentration of terephthalic acid was less than 1 ug/ml. However, the presence of trace levels of terephthalic acid was detected in the blood throughout the post-exposure recovery period.

Reference: Amoco Corporation (1989) Time Course Analysis of Terephthalic Acid Concentration in Blood and Urine of Rats Following Inhalation Exposures. Study IITRI Study #1448A

Type: Adsorption

Remark: Hoshi and Kuretani (1967) characterized the gastrointestinal absorption of [14C-carboxyl]-terephthalic acid in female Wistar rat given a single gavage dose of 85 mg/kg. The compound was administered to groups of five rats as a suspension in a 0.5% sodium carboxymethylcellulose. The esophagus, stomach, small intestine, cecum and large intestine of rats were assayed for radioactivity 2, 4, 6, 8, 24 and 48 hours after administration. Urine and feces were collected from treated rats after 8, 24 and 48 hours, and assayed for radioactivity. Expired air and feces collected for 24 hours accounted for <0.04 and 3.3% of the total radioactivity administrated, respectively. The dose was absorbed rapidly, as it was excreted in the urine almost quantitatively by 24 hours. CO_2 as the cleavage product was not found in the expired air. After examining the various gastrointestinal segments, the authors calculated that 70 and 26% of the administered dose was absorbed from the upper (i.e. stomach and small intestine) and lower (i.e., cecum and

large intestine) portions, respectively. No metabolites were detected in the urine.

Reference: Hoshi A, Kuretani K. (1967) Metabolism of terephthalic acid III. Absorption of terephthalic acid from the gastrointestinal tract and detection of its metabolites. Chem Pharm Bull 15, 1979-1984

Type: Distribution

Remark: Hoshi and Kuretani (1968) studied the distribution of [14C -carboxyl]-terephthalic acid in the female Wistar rat. Groups of five animals were given a single gavage dose of 85 mg terephthalic acid suspended in 0.5% sodium carboxymethylcellulose. Animals were killed and their blood and tissues assayed for radioactivity 2, 4, 6, 8, 24 and 48 hours after administration. Samples of plasma, kidney, liver, brain, skin, lung, pancreas, spleen, fat, heart, muscle, bone, erythrocytes, uterus, ovary and endocrine glands contained terephthalic acid up to 6 hours after administration, with the kidney having the highest concentrations, followed by the liver and plasma. No radioactivity was observed in any of the above tissues 48 hours after administration. The biological half-life of terephthalic acid in these tissues was 1.2-3.3 hours, and elimination followed first-order kinetics. Similar results were observed in rats and fed a diet containing 0.5% [14C-carboxyl]-terephthalic acid for 1 or 3 days, and killed immediately or 1 day after exposure. These results showed that terephthalic acid was widely distributed in various body tissues, but did not accumulate in any of them.

Reference: Hoshi A, Kuretani K. (1968) Distribution of terphthalic acid in tissues. Chem Pharm Bull 16, 131-135

Type: Distribution

Remark: Adult male rats were administered single (0-80 mg/kg 14C-terephthalic acid) or multiple (5 doses totalling 0-80 mg/kg 14C-terephthalic acid over 10 days) oral doses. It was found that more than 80% of a single dose of 14C-terephthalic acid was excreted in the urine and feces within 48 hours of administration. After repeated dosing, more than 89% of the total administered was recovered in the urine and feces within 24 hours of the last dose. Negligible tissue absorption and accumulation in organs were recorded. Forty-eight hours after a single intratracheal dose (0-10 mg/kg), rats excreted 49-73% of the total administered; 45-66.6% was recovered in the urine and 3.4-6.4% in the feces. After repeated intratracheal exposures (5 doses totalling 0-10 mg/kg), less than one percent of the total dose was found in the lungs and tracheal lymph nodes, 24 hours after the last treatment. Insignificant amounts of terephthalic acid were detected in the other organs assayed.
Dermal and ocular application of terephthalic acid revealed negligible excretion and absorption following single, multiple, or long term exposure. The direct instillation of up to 10 mg radio labelled terephthalic acid (as a 1% solution in emulsified distilled water) into the lungs of rats, five times in 10 days produced no evidence of accumulation. Less than 1% of the administered dose was present in the lungs and windpipe lymph nodes 24 hr after the final instillation. Negligible radioactivity (< 0.1% of dose) was detected in the other organs assayed.

Reference: Hoshi A, Yanai R, Kuretani K. (1968) Toxicity of terephthalic acid Chem Pharm Bull 16 1655-1660

Type: Excretion

Remark: Hoshi and Kuretani (1965) studied the excretion of terephthalic acid when given to rats by gavage, intraperitoneal injection and dietary inclusion. when a gavage dose of 200 mg terephthalic acid per kg suspended in 0.5% aqueous sodium carboxymethylcellulose was given to rats, terephthalic acid was found 24 hours after administration in the urine and feces, and accounted for about 55 and 30% of the dose, respectively. When a similar dose was given by intraperitoneal injection, most of the dose was recovered quantitatively in the urine after 24 hours. When fed 300 mg

terephthalic acid/kg/day, rats excreted 78-85% of the dose in urine and the rest in feces by 24 hours after feeding.

Reference: Hoshi A, Kuretani K. (1965) Metabolism of terphthalic acid I. Excretion of terephthalic acid in urine. Yakugaku Zasshi 85, 905-908

Type: Excretion

Remark: By use of the Sperber in vivo chicken preparation method, infusion of radiolabeled terephthalic acid ([14C]TPA) into the renal portal circulation revealed a first-pass excretion of the unchanged compound into the urine. This model was utilized further to characterize the excretory transport of [14C]TPA and provide information on the structural specificity in the secretion of dicarboxylic acids. At an infusion rate of 0.4 nmol/min 60% of the [14C]TPA which reached the kidney was directly excreted. An infusion rate of 3 or 6 nmol/min resulted in complete removal of [14C]TPA by the kidney. These results indicate that TPA is both actively secreted and reabsorbed when infused at 0.4 nmol/min and that active reabsorption is saturated with the infusion of TPA at higher concentrations. The secretory process was saturated with the infusion of TPA at 40 nmol/min. The excretory transport of TPA was inhibited by the infusion of probenecid, salicylate, and m-hydroxybenzoic acid, indicating that these organic acids share the same organic anion excretory transport process. m-Hydroxybenzoic acid did not alter the simultaneously measured excretory transport of p-aminohippuric acid (PAH), suggesting that there are different systems involved in the secretion of TPA and PAH. The structural specificity for renal secretion of dicarboxylic acids was revealed by the use of o-phthalic acid and m-phthalic acid as possible inhibitors of TPA secretion. m-Phthalate, but not o-phthalate, inhibited TPA excretory transport, indicating that there is some specificity in the renal secretion of carboxy-substituted benzoic acids. TPA was actively accumulated by rat and human cadaver renal cortical slices.

Reference: Tremaine LM, Quebbemann AJ. (1985) The renal handling of terephthalic acid. Toxicol Appl Pharmacol 77(1), 165-74

Type: Metabolism

Remark: The induction of calcium terephthalate (CaTPA) calculi in the urinary tract of rats ingesting terephthalic acid (TPA) or dimethylterephthalate is a result of supersaturation with respect to the stone components. The solubility product of CaTPA was determined in water at 37 degrees C, and it value in urine of exposed weanling Fischer-344 rats was calculated based on the electrolyte concentrations of freshly-collected, microliter urine samples. The value of the solubility product in urine is equal to the minimum concentration product of free Ca and TPA at which crystallization can occur; hence, the urinary solubility product is a parameter that is useful for risk assessment. Estimates of the TPA concentrations required to induce crystals or stones in normal human urine are presented.

Reference: Heck Hd'A (1981) Chemical urolithiasis 2. Thermodynamic aspects of bladder stone induction by terephthalic acid and dimethyl terephthalate in weanling Fischer-344 rats. Fundam Appl Toxicol 1(4), 299-308

Type: Toxicokinetics

Remark: The pharmacokinetics of [14C]terephthalic acid ([14C]TPA)were determined in Fischer-344 rats after intravenous and oral administration. After iv injection, the plasma concentration-time data were fitted using a three-compartment pharmacokinetic model. The average terminal half-life in three rats was 1.2 +/- 0.4 hr, and the average volume of distribution of the terminal phase was 1.3 +/- 0.3 liters/kg. Following administration by gavage, a longer terminal half-life was obtained, indicating that dissolution of [14C]TPA or absorption from the gut may be partially rate-limiting. Recovery of [14C]TPA in the urine following a bolus iv dose was 101 +/- 8%, indicating essentially complete urinary excretion of the compound. No evidence of metabolism of [14C]TPA was obtained by analysis of urine by high-performance liquid chromatography. [14C]TPA was

transported to the fetus after administration of the compound to pregnant rats; however, the concentrations in fetal tissues were low relative to the corresponding maternal tissues. Neonatal rats exposed to 5% TPA in the diet of their dams did not develop calculi until the onset of self-feeding. These results demonstrate that TPA is rapidly excreted into urine after administration to rats, and that excretory mechanisms in the dam provide an effective mechanism of defense against TPA-induced urolithiasis in neonatal rats.

Reference: Wolkowski-Tyl R, Chin TY, Heck Hd'A (1982) Chemical urolithiasis. 3. Pharmacokinetics and transplacental transport of terephthalic acid in Fischer-344 rats. Drug Metab Dispos 10, 486-490

Type: Toxicokinetics

Remark: Changes of terephthalic acid (TPA) concentration in blood plasma was detected in the rabbit and the rat. TPA, when injected i.p., was rapidly absorbed into the plasma and then excreted. The TPA concentration in plasma reached a maximum level within 1 hour after injection, decreased gradually, and was not found after 24 hrs. The half-life of TPA in plasma was 1.8 hrs. When a TPA suspension was orally administered in doses of 200 and 100 mg/kg, the TPA concentration in plasma reached a maximum level within 8-10 hrs., and decreased slowly. In this case, the TPA concentration in plasma was very low, being only 11.7 ug/ml, at the 8th hour after the administration of 200 mg/kg. The half-life of TPA in plasma after its oral administration was 27 hours In the rat, the half-life of TPA in plasma was 1 hour, and 3.4 hours, in cases of intraperitoneal and oral administrations respectively.

Reference: Hoshi A, Yanai R, Kuretani K. (1968) Metabolism of terephthalic acid II. Plasma concentration of terephthalic acid and its biological half-life. Yakugaku Zasshi 86 963-967 [Chem Abstr 66 9665 1967]

Type: Toxicokinetics

Remark: Maternal and fetal tissue distributions in rats of [14C]terephthalic acid were determined by serial killings of pregnant animals (gestation 20) at 0.75, 2.5, 4, 7, 10, and 12 hours after a single oral dose of [14C]terephthalic acid, and by whole body autoradiography at 3 and 5.5 hours. Placental transport of terephthalic acid to and elimination from the fetus is slow relative to elimination from the dam. Accumulation of radioactivity was noted in both fetal and maternal liver, kidney, and bladder.

Reference: Wolkowski-Tyl R, Chin TY, Heck Hd'A (1982) Chemical urolithiasis. 3. Pharmacokinetics and transplacental transport of terephthalic acid in Fischer-344 rats. Drug Metab Dispos 10, 486-490

Type: Toxicokinetics

Remark: Between 20 and 40% of the terephthalic acid fed to rats is absorbed and excreted by the kidney. Only 6% of the acid is not excreted in the urine, but appeared in the feces. The remainder is probably destroyed in the gut rather than absorbed and either metabolized or stored in the tissues.

Reference: DuPont. Unpublished study, MR 468-1

Type: Risk Assessment

Based on urinary solubility of terephthalic acid, normal human urine would become saturated with calcium-terephthalate at a terephthalic concentration of approximately 8 to 16 mM.

Assuming that the average volume of urine excreted by humans is 1.5 liters/day, the amount of terephthalic acid that would have to be absorbed to produce the minimum saturating concentration of terephthalic acid is 2400 mg/day.

Reference: Heck, H. d'A., and Tyl, R.W. (1985) The induction of bladder stones by terephthalic acid, dimethyl terepthalate, and melamine (2,4,6-triamino-s-triazine and its relevance to risk assessment. Regul. Toxicol. Pharmacol. 5, 294-313.

5.11 EXPERIENCE WITH HUMAN EXPOSURE

Remark:	A 10 ml application of an oily paste containing 80% terephthalic acid to equal sites on the hand was not irritating. Also, a 24 hour application did not produce any signs of irritation or redness.
Reference:	Massman. (1966) Inst Fuer Arbeitsmedizin der Uni Tuebingen, 1966

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IUCLID DATASET FOR

TEREPHTHALIC ACID (CAS RN 100-21-0)

I U C L I D

D a t a s e t

Existing Chemical	Substance ID: 100-21-0
CAS No.	100-21-0
EINECS Name	terephthalic acid
EINECS No.	202-830-0
Molecular Formula	C8H6O4

Dataset created by: EUROPEAN COMMISSION - European Chemicals Bureau

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Country: France
Telex: 04 72 73 95 00

Name: SIPET SpA
Street: Via Morolense Km 10
Town: 03010 Patrica (FR)
Country: Italy
Phone: +39-0775-842211

Name: TRANSOL CHEMICALS BV
Street: POSTBUS 1030
Town: 2980BA RIDDERKERK
Country: Netherlands
Phone: 0180-460300
Telefax: 0180-417310

1.0.2 Location of Production Site

-

1.0.3 Identity of Recipients

-

1.1 General Substance Information

Substance type: organic
Physical status: solid

Substance type:
Physical status:

1.1.1 Spectra

-

1.2 Synonyms

1,4 - Benzenedicarboxylic acid.
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

1,4-Benzenedicarboxylic acid (9CI)
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

1,4-Dicarboxybenzene
Source: Amoco Chemical Company Gerrards Cross
BASF AG Ludwigshafen

Acide benz¿nedicarboxilique 1-4
Source: Rhodia Belle Etoile SAS St Fons

Acide p-phtalique
Source: Rhodia Belle Etoile SAS St Fons

Benzeen-p-dicarboxylic zuur
Source: TRANSOL CHEMICALS BV RIDDERKERK

Benzene-1,4-dicarboxylic acid
Source: AGFA - Gevaert N.V. Mortsel-België

p-Benzenedicarboxylic acid
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
Amoco Chemical Company Gerrards Cross
BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

p-Carboxybenzoic acid
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
Amoco Chemical Company Gerrards Cross
BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

p-Dicarboxybenzene
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
Amoco Chemical Company Gerrards Cross
BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

p-Phthalic acid
Source: Amoco Chemical Company Gerrards Cross
BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

PTA
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

PTA, 1-4 acido benzenedicarbossilico
Source: SIPET SpA Patrica (FR)

Pure Terephthalic acid
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

Synonym a: PTA
Source: PCK AG Schwedt Schwedt/Oder
PCK Raffinerie GmbH Schwedt Schwedt/Oder

Synonym c: Benzen-p-dicarbonsäure
Source: PCK Raffinerie GmbH Schwedt Schwedt/Oder

Terephthalic acid
Source: AGFA - Gevaert N.V. Mortsel-België
Amoco Chemical Company Gerrards Cross

Terephthalic acid (7CI, 8CI)
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

Terephthalic acid - TPA
Source: Enichem Fibre S.p.A. Milan

TEREPHTHALIC ACID, TPA.
Source: INCA INTERNATIONAL S.p.A. Milan

Terephthalsaeure
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

TPA
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
Amoco Chemical Company Gerrards Cross
BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

WR 16262
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity

Quantity more than 1 000 000 tonnes

1.6.1 Labelling
-

1.6.2 Classification
-

1.7 Use Pattern

Type: type
Category: Non dispersive use

Type: type
Category: Use in closed system

Type: type
Category: Use resulting in inclusion into or onto matrix

Type: industrial
Category: Agricultural industry

Type: industrial
Category: Basic industry: basic chemicals

Type: industrial
Category: Chemical industry: used in synthesis

Type: industrial
Category: Paints, lacquers and varnishes industry

Type: industrial
Category: Polymers industry

Type: industrial
Category: Textile processing industry

Type: use
Category: Adhesive, binding agents

Type: use
Category: Intermediates

Type: use
Category: other: Manufacture of polyethyleneterephthalate

Type: use
Category: other: Monomeres

Type: use
Category: other

1.7.1 Technology Production/Use

-

1.8 Occupational Exposure Limit Values

Type of limit: MAK (DE)
Limit value:
Remark: Stoffliste b) Stoffe, fuer die (noch) keine MAK-Werte aufgestellt werden koennen
Source: Hoechst AG Frankfurt/Main

(1)

Type of limit: MAK (DE)
Limit value: 6 mg/m3
Remark: Allgemeiner Staubgrenzwert, festgesetzt als Feinstaubkonzentration
¿
Source: PCK AG Schwedt Schwedt/Oder

(2)

Type of limit: MAK (DE)
Limit value:
Remark: Stoffliste IIb (kann derzeit kein MAK-Wert aufgestellt werden)
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(3)

Type of limit: MAK (DE)
Limit value: 6 mg/m3
Remark: Allgemeiner Staubgrenzwert, festgesetzt als Feinstaubkonzentration
¿
Source: PCK Raffinerie GmbH Schwedt Schwedt/Oder

(4)

Type of limit: TLV (US)
Limit value: 10 mg/m3
Remark: In our plant mean concentration in air of workplace is 1.68mg/m3.
Source: INCA INTERNATIONAL S.p.A. Milan

Type of limit: TLV (US)
Limit value: 10 mg/m3
Remark: In our plant mean concentration in air of workplace is 1.68 mg/mc.
Source: Enichem Fibre S.p.A. Milan

Type of limit: TLV (US)
Limit value: 10 mg/m3
Remark: STEL value not available
Source: SIPET SpA Patrica (FR)

Type of limit: TLV (US)
Limit value: 10 mg/m3
Source: Amoco Chemical Company Gerrards Cross

Type of limit:
Limit value:
Remark: None
Source: AGFA - Gevaert N.V. Mortsel-België

Type of limit:
Limit value:
Remark: Sensitization and intolerance.-
A standard text states that terephthalic acid is 'not a [skin] sensitizer' [but provides no further detalis] (Patty, 1963).
General Systemic effects.-
Single exposure
Non-human. Oral. LD50: > 6.4 g/kg bw (Marhold, 1972; Petty, 1963).
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

1.9 Source of Exposure

Remark: Production in our plant is performed in substantially closed system and the chemical is 100% intermediate. It is used in the same factory, or others, practically only for preparation of the polyester polymer (no public use). Moderate release occurs from drying process, actually 10 Kg/h.
Source: INCA INTERNATIONAL S.p.A. Milan

Remark: Production in our plant is performed in substantially closed system and the chemical is 100 % intermediate. It is used in the same factory, or others, practically only for preparation of the polyester polymer (no public use). Moderate release occurs from drying process, actually 10 Kg/h.
Source: Enichem Fibre S.p.A. Milan

Remark: Exposure source:

During the PTA's containers unloading
Source: SIPET SpA Patrica (FR)

Remark: Die Terephthalsäureherstellung erfolgt nach einer Lizenz der Fa. Amoco in 2 Prozeßstufen. Die Herstellung der Roh-Terephthalsäure erfolgt in der homogenkatalytischen Flüssigphasenoxidation von p-Xylol in Essigsäure mit dem Katalysatorsystem Kobalt-, Mangan- und Bromidionen. Anschließend erfolgt die Reinigung der Roh-Terephthalsäure durch Hydrierung an einem Palladium-Aktivkohlekatalysator mit nachgeschalteter Kristallisation. ¿
Source: PCK AG Schwedt Schwedt/Oder

Remark: Die Terephthalsäureherstellung erfolgt nach einer Lizenz der Fa. Amoco in 2 Prozeßstufen. Die Herstellung der Roh-Terephthalsäure erfolgt in der homogenkatalytischen Flüssigphasenoxidation von p-Xylol in Essigsäure mit dem Katalysatorsystem Kobalt-, Mangan- und Bromidionen. Anschließend erfolgt die Reinigung der Roh-Terephthalsäure durch Hydrierung an einem Palladium-Aktivkohlekatalysator mit nachgeschalteter Kristallisation. ¿
Source: PCK Raffinerie GmbH Schwedt Schwedt/Oder

1.10.1 Recommendations/Precautionary Measures

–

1.10.2 Emergency Measures

–

1.11 Packaging

–

1.12 Possib. of Rendering Subst. Harmless

-

1.13 Statements Concerning Waste

-

1.14.1 Water Pollution

Classified by: other: Hoechst AG
Labelled by: other: Hoechst AG
Class of danger: 1 (weakly water polluting)
Source: Hoechst AG Frankfurt/Main

(5)

Classified by: other: Wassergefährdungsklasse (WGK)
Labelled by:
Class of danger: 0 (generally not water polluting)
Remark: Selbsteinstufung
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(6)

1.14.2 Major Accident Hazards

Legislation: Stoerfallverordnung (DE)
Substance listed: no
Source: Hoechst AG Frankfurt/Main

(7)

Legislation: Stoerfallverordnung (DE)
Substance listed: no
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(8)

1.14.3 Air Pollution

Classified by: TA-Luft (DE)
Labelled by:
Number: 3.1.7 (organic substances)
Class of danger: III
Remark: Selbsteinstufung
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(9)

Classified by: other: Hoechst AG
Labelled by: other: Hoechst AG
Number: 3.1.7 (organic substances)
Class of danger: III
Source: Hoechst AG Frankfurt/Main

(10)

1.15 Additional Remarks

Remark: Material may be disposed in an approved chemical incinerator. If facilities are not available or practical, material may be buried in an approved waste chemical landfill. When dilute with water, it is amenable to biological treatment at a industrial sewage treatment plant.
Source: INCA INTERNATIONAL S.p.A. Milan

Remark: Material may be disposal in an approved chemical incinerator. If facilities are not available or practical, material may be buried in an approved waste chemical landfill. When dilute with water, it is amenable to biological treatment at a industrial sewage treatment plant.
Source: Enichem Fibre S.p.A. Milan

1.16 Last Literature Search

-

1.17 Reviews

-

1.18 Listings e.g. Chemical Inventories

-

2.1 Melting Point

Value: > 300 degree C
Sublimation: yes
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Value: > 300 degree C
Decomposition: no
Sublimation: yes
Method: other
GLP: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(11)

Value: = 402 degree C
Sublimation: yes
Method: other
GLP: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(12)

Value: = 402 degree C
Sublimation: yes
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(13)

Value: 425 degree C
Decomposition: no
Sublimation: no
Method: other
GLP: no data
Remark: Measured in sealed tube.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(14)

Value: = 425 degree C
Remark: In geschlossenem Röhrchen
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15)

Value:
Sublimation: yes
Method: other
GLP: no data
Remark: It sublimates above 300°C (at 101.3 Kpa) without melting.
Source: INCA INTERNATIONAL S.p.A. Milan
(16)

Value:
Decomposition: no
Sublimation: yes
Remark: Subliamtion without melting at 300 °C and 103.1 kPa
Source: SIPET SpA Patrica (FR)

2.2 Boiling Point

Value:
Remark: Sublima a 299 °C
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Value:
Remark: It sublimates above 300°C (at 101.3 Kpa) without melting.
Source: INCA INTERNATIONAL S.p.A. Milan
(17)

Value:
Remark: Sublimation happen at atmospheric pressure
Source: SIPET SpA Patrica (FR)

2.3 Density

Type: density
Value: = 1.51 g/cm3 at 20 degree C
Source: SIPET SpA Patrica (FR)

Type: density
Value: = 1510 kg/m3 at 20 degree C
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Type: density
Value: = 1.4 g/cm3 at 25 degree C
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15)

Type: bulk density
Value: 1.12 g/cm3
Method: other: DIN 5314
GLP: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(14)

Type: density
Value: 1.5 g/cm3
Method: other
GLP: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(14)

Type: relative density
Value: = 1.51
Method: other
GLP: no data
Source: INCA INTERNATIONAL S.p.A. Milan
(18)

Type: density
Value: 1.51 g/cm3
Method: other
GLP: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(12)

2.3.1 Granulometry

-

2.4 Vapour Pressure

Value: = 0 - 134633 hPa at 20 degree C
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Value: = .00000000003 hPa at 20 degree C
Remark: Extrapoliert aus nur im Temperaturbereich von 249.85 bis 427.0 °C gültigen Dampfdruckwerten. Die in der Literatur genannten abweichenden Dampfdruckwerte beziehen sich auf Messungen älteren Datums.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(19)

Value: = .0000000003 hPa at 20 degree C
GLP: no data
Remark: Value extrapolated from vapour pressures measured at temperatures between 250 and 427 Deg C.

Other values quoted in the literature have been generated using old test methods.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(20)

Value: 1.33 at 78 degree C
GLP: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(21)

Value: = 6.26 hPa at 150 degree C
Method: other (measured)
GLP: no data
Source: INCA INTERNATIONAL S.p.A. Milan
(22)

Value: = 6.26 hPa at 150 degree C
Source: SIPET SpA Patrica (FR)

Value: = 13 hPa at 304 degree C
GLP: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(14)

Value: = 13 hPa at 304 degree C
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15)

2.5 Partition Coefficient

log Pow: = 1.16
Method:
Year:
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(23)

log Pow: = 1.19
Method: other (calculated)
Year:
GLP: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(24)

log Pow: = 1.25 at 25 degree C
Method:
Year:
Remark: Ottanolo/acqua
Source: SIPET SpA Patrica (FR)

log Pow: = 1.25 at 25 degree C
Method: other (measured)
Year:
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(25)

log Pow: = 1.25 at 25 degree C
Method: other (measured): Schüttelmethode
Year:
GLP: no data
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(26)

log Pow: = 1.96
Method: other (measured)
Year:
GLP: no data
Remark: TPA has ionic nature. For this measure is unknown pH of the experimentation.
Source: INCA INTERNATIONAL S.p.A. Milan
Test condition: Shaking method.
(27)

log Pow: = 1.96
Method: other (measured)
Year:
GLP: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(28)

log Pow: = 1.96
Method: other (measured): Schüttelmethode
Year:
GLP: no data
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(29)

log Pow: 2
Method: other (measured)
Year:
GLP: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(30)

log Pow: = 2
Method: other (measured): Schüttelmethode
Year:
GLP: no data
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(31)

2.6.1 Water Solubility

Value: 15 mg/l at 10 degree C
Qualitative: not soluble
Method: other
GLP: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(14)

Value: = 15 mg/l at 10 degree C
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15)

Value: = 19 mg/l at 25 degree C
pKa: 3.52 at 25 degree C
Method: other
GLP: no data
Remark: pKa1 = 3.52 at 25°C
pKa2 = 4.46 at 25°C
Water solubilyty: TPA has ionic nature. For this measure is unknown pH of the experimentation.
Source: INCA INTERNATIONAL S.p.A. Milan
(32) (33)

Value: = 19 mg/l at 25 degree C
Source: SIPET SpA Patrica (FR)

Value: = 19 mg/l at 25 degree C
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(34)

Value: 19 mg/l
Qualitative: not soluble
Method: other
GLP: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(11)

pKa: 3.52 at 25 degree C
Method: other
GLP: no data
Remark: pKa1
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(11)

pKa: 4.46 at 25 degree C
Remark: pKa2
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(11)

pKa: 3.54 at 25 degree C
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(35)

pKa: 4.46 at 25 degree C
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(35)

Remark: Dissoziationskonstanten: 20 °C: pka1: 3.5; pka2: 4.34
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(36)

2.6.2 Surface Tension

–

2.7 Flash Point

Value: = 260 degree C
Type: open cup
Method: other
Year:
GLP: no data
Source: INCA INTERNATIONAL S.p.A. Milan
(37)

Value: = 680 degree C
Type:
Method:
Year:
Remark: Porcentaje límite de O2 (ignición por chispa) : 15
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Value:
Type:
Method:
Year:
Remark: Not applicable
Source: SIPET SpA Patrica (FR)

2.8 Auto Flammability

Value: = 496 degree C
Source: SIPET SpA Patrica (FR)

Value: = 680 degree C
Method: other
GLP: no data
Remark: 680°C as a dust cloud (ignition).
Source: INCA INTERNATIONAL S.p.A. Milan

(38)

2.9 Flammability

Result: other
Remark: None flammability classification
Source: SIPET SpA Patrica (FR)

Result:
Remark: Productos de combustión: CO -- CO2 -- Agua
Productos de extinción: Agua pulverizada-Polvo-Espuma CO2 y Halón.
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

2.10 Explosive Properties

Result: not explosive
Method: other
GLP: no data
Remark: Explosivity in air : Lower Limit = 0.05 g/l
Source: INCA INTERNATIONAL S.p.A. Milan

(39)

Result: other
Remark: High dust concentrations have a potential for combustion or explosion
Source: SIPET SpA Patrica (FR)

Result:
Remark: Concentración mínima para la explosión Kg/m3 : 0.050
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Result:
Remark: Untere Explosionsgrenze: 40 g/m3 in Luft
Obere Explosionsgrenze: keine
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15)

2.11 Oxidizing Properties

Result: no oxidizing properties
Source: SIPET SpA Patrica (FR)

2.12 Additional Remarks

Remark: Lower flammable limit: 40 g/m3
Flammable powder class: A
Minimum ignition temperature: 500 Deg C
Minimum ignition energy: 50 mJ
Sublimation temperature: 300 Deg C
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(14)

Remark: Untere Explosionsgrenze: 40 g/m3 in Luft
Obere Explosionsgrenze: keine
Zündenergie: 50 ml
Gefährliche Zersetzungsprodukte/Reaktionen: Bei Vorhandensein von Staub, fein verteilter Terephthalsäure und einer Zündquelle kann eine Staubexplosion ausgelöst werden.
Thermische Zersetzung: CO2 + H2O
Keine Luft für Druckluftfördergebläse, sondern Schutzgas mit einem Sauerstoffanteil von weniger als 8 % verwenden.
Zündtemperatur: 650 °C
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(15)

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500000 molecule/cm3
Rate constant: = .0000000000002 cm3/(molecule * sec)
Degradation: = 50 % after 79 day
Method: other (calculated): Atkinson
Year: **GLP:**
Test substance:
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(40)

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 1500000 molecule/cm3
Rate constant: = .0000000000010027 cm3/(molecule * sec)
Degradation: ca. 50 % after 10.7 day
Method: other (calculated): AOPWIN, Version 1.55, April 1994, Syracruse Res.; nach Atkinson
Year: **GLP:**
Test substance:
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(41)

Type:
Method:
Year: **GLP:**
Test substance:
Remark: Es biodegradable.
Relevant phisical properties: a crystalline solic, practically insoluble in water, chloroform or other. Slighly soluble in cold ethanol (Merck, 1983).
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Type:
Method:
Year: **GLP:**
Test substance:
Source: SIPET SpA Patrica (FR)

3.1.2 Stability in Water

–

3.1.3 Stability in Soil

–

3.2 Monitoring Data (Environment)

Type of measurement: other: Atmosphaere
Medium:
Remark: Konzentrationen von 11.1 ng TPA/m3 (Durchschnitt 6 Tage) wurden in Japan in der Atmosphaere gemessen, der Maximalwert betrug 23 ng/m3. Die TPA wurde wahrscheinlich aus Kohlenwasserstoffen durch photochemische Reaktionen gebildet.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(42)

Type of measurement: other: Atmosphäre
Medium:
Remark: Konzentrationen von 11.1 ng TPA/m3 (Durchschnitt 6 Tage) wurden in Japan in der Atmosphäre gemessen, der Maximalwert betrug 23 ng/m3. Die TPA wurde wahrscheinlich aus Kohlenwasserstoffen durch photochemische Reaktionen gebildet.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(42)

Type of measurement: other: Fluesse
Medium:
Remark: In Japan wurden 1975 TPA-Konzentrationen von bis zu 3.4 ug/l Flusswasser gefunden.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(43)

Type of measurement: other: Flüsse
Medium:
Remark: In Japan wurden 1975 TPA-Konzentrationen von bis zu 3.4 µg/l Flußwasser gefunden.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(43)

Type of measurement: other: Klaeranlagenablauf
Medium:
Remark: Im Ablauf einer kommunalen Klaeranlage wurde 1975 in der USA (Washington DC) eine TPA-Konzentration von ca. 13 ng/l gefunden.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(44)

Type of measurement: other: Klaeranlagenablauf
Medium:
Remark: In Japan wurden 1975 TPA-Konzentrationen von bis zu 5.3 ug/l im Ablauf einer kommunalen Klaeranlage gefunden.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(43)

Type of measurement: other: Klaerschlamm
Medium:
Remark: In der BRD konnte 1984 im Klaerschlamm einer gewerblich/ kommunalen Klaeranlage TPA qualitativ nachgewiesen werden.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(45)

Type of measurement: other: Kläranlagenablauf
Medium:
Remark: Im Ablauf einer kommunalen Kläranlage wurde 1975 in der USA (Washington DC) eine TPA-Konzentration von ca. 13 ng/l gefunden.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(44)

Type of measurement: other: Kläranlagenablauf
Medium:
Remark: In Japan wurden 1975 TPA-Konzentrationen von bis zu 5.3 µg/l im Ablauf einer kommunalen Kläranlage gefunden.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(43)

Type of measurement: other: Klärschlamm
Medium:
Remark: In der BRD konnte 1984 im Klärschlamm einer gewerblich/ kommunalen Kläranlage TPA qualitativ nachgewiesen werden.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(46)

Type of measurement: other: Meereskueste
Medium:
Remark: In Japan wurden in 6 von 100 Meerwasserproben TPA mit einer durchschnittlichen Konzentration von 0.7 ug/l nachgewiesen. Die Probenentnahmen erfolgten zwischen 1974 und 1976 im Kuestenbereich von Industriegebieten.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(47)

Type of measurement: other: Meeresküste
Medium:
Remark: In Japan wurden in 6 von 100 Meerwasserproben TPA mit einer durchschnittlichen Konzentration von 0.7 µg/l nachgewiesen. Die Probenentnahmen erfolgten zwischen 1974 und 1976 im Küstenbereich von Industriegebieten.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(47)

Type of measurement: other: Pflanzen
Medium:
Remark: Vorkommen:
Natuerlich in Kreuzdorngewaechsen (Rhamnaceae, Zizyphus sativa)
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(48)

Type of measurement: other: Pflanzen
Medium:
Remark: Vorkommen: Natürlich in Kreuzdorngewächsen (Rhamnaceae, Zizyphus sativa)
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(48)

Type of measurement:
Medium:
Source: SIPET SpA Patrica (FR)

3.3.1 Transport between Environmental Compartments

Type: adsorption
Media: other
Method: other
Year: 1988
Remark: Method calculated
KOC not estimated
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(49)

3.3.2 Distribution

Media: air - biota - sediment(s) - soil - water
Method: other (calculation)
Year: 1993
Method: Enichem Computer program by Garlanda T. and Masoero M.
Remark: Theoretical distribution between environmental compartments calculated on a global basis . The model represents a steady-state partitioning, not including reaction or interphase transport. Applications and limitations are the same as for a fugacity model of I level. In the present case the ratio between the soil-water areas is 70/30.
Result:

Percent in air	: 8.83*10(E-11)
Percent in water	: 97.1
Percent in soil	: 1.48
Percent in sediment	: 1.39

Source: INCA INTERNATIONAL S.p.A. Milan
Test condition:

Molecular mass	: 166.13
Melting point	: 300°C
Water solubility	: 19.0 mg/l
Vapor pressure (calculated)	: 3*10(E-13) Pa a 25°C
Temperature	: 298 °Kelvin
log Kow	: 1.96 *

* Reported in Alstoff Information Datebank (AIDA) from Dunn, W.J., Johansson, E., (1983): Quant. Struct.-Act. Relat. 2, 156-163.

TPA has an ionic nature. The distribution is calculated on the basis of data attribuited to free acid.

3.4 Mode of Degradation in Actual Use

-

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge, adapted
Degradation: = 72 % after 28 day
Method: OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
Year: **GLP:** no data
Test substance: no data
Remark: Versuchsdurchfuehrung gemaess der von Sturm 1973 vorgeschlagenen Methode.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire

(50)

Type: aerobic
Inoculum: activated sludge, adapted
Degradation: = 72 % after 28 day
Method: OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
Year: **GLP:** no data
Test substance: no data
Remark: Versuchsdurchführung gemäß der von Sturm 1973 vorgeschlagenen Methode.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(50)

Type: aerobic
Inoculum: activated sludge, adapted
Degradation: = 91 % after 28 day
Method: OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
Year: **GLP:** no data
Test substance: no data
Remark: Versuchsdurchfuehrung gemaess der von Sturm 1973 vorgeschlagenen Methode.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(50)

Type: aerobic
Inoculum: activated sludge, adapted
Degradation: = 91 % after 28 day
Method: OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
Year: **GLP:** no data
Test substance: no data
Remark: Versuchsdurchführung gemäß der von Sturm 1973 vorgeschlagenen Methode.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(50)

Type: aerobic
Inoculum: domestic sewage
Concentration: 20 mg/l related to Test substance
Degradation: > 60 % after 10 day
Result: readily biodegradable
Method: OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
Year: 1992 **GLP:** yes
Test substance: no data
Source: INCA INTERNATIONAL S.p.A. Milan
(51)

Type: aerobic
Inoculum: domestic sewage, non-adapted
Concentration: 20 mg/l related to Test substance
Degradation: > 60 % after 10 day
Result: readily biodegradable
Method: OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
Year: 1992 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: A value of >60% degredation was also obtained with a nominal initial concentration of 10mg/l terephthalic acid.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(52)

Type: aerobic
Inoculum: activated sludge, non-adapted
Degradation: after 30 day
Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year: **GLP:** no data
Test substance: no data
Remark: Versuchsdurchfuehrung gemaess Stand 1974; Abbaugrad nach 30 d: 112 %
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
Test condition: 1 Tropfen/l

(50)

Type: aerobic
Inoculum: activated sludge, non-adapted
Degradation: after 30 day
Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year: **GLP:** no data
Test substance: no data
Remark: Versuchsdurchführung gemäß Stand 1974; Abbaugrad nach 30 d: 112 %
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
Test condition: 1 Tropfen/l

(50)

Type: aerobic
Inoculum: other: Schluffiger Lehm
Concentration: 20 mg/l related to Test substance
Degradation: = 100 % after 2 day
Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year: **GLP:** no data
Test substance: no data
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(53)

Type: aerobic
Inoculum: predominantly domestic sewage
Degradation: = 82 % after 19 day
Method: OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
Year: **GLP:** no data
Test substance: no data
Remark: Versuchsdurchfuehrung gemaess der von OECD 1976 vorgeschlagenen Methode.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(50)

Type: aerobic
Inoculum: predominantly domestic sewage
Degradation: = 82 % after 19 day
Method: OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
Year: **GLP:** no data
Test substance: no data
Remark: Versuchsdurchführung gemäß der von OECD 1976 vorgeschlagenen Methode.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(50)

Type: aerobic
Inoculum: activated sludge, industrial, non-adapted
Concentration: related to Test substance
Degradation: = 98 % after 6 day
Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: **GLP:** no data
Test substance: no data
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(54)

Type: aerobic
Inoculum: activated sludge, non-adapted
Degradation: = 93 % after 4 day
Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: **GLP:** no data
Test substance: no data
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(50)

Type: aerobic
Inoculum: activated sludge, non-adapted
Degradation: = 93 % after 1 day
Method: OECD Guide-line 303 A "Simulation Test - Aerobic Sewage Treatment: Coupled Unit Test"
Year: **GLP:** no data
Test substance: no data
Remark: Versuchsdurchfuehrung in Anlehnung an den OECD-Confirmatory Test Stand 1976.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(50)

Type: aerobic
Inoculum: activated sludge, non-adapted
Degradation: = 93 % after 1 day
Method: OECD Guide-line 303 A "Simulation Test - Aerobic Sewage Treatment: Coupled Unit Test"
Year: **GLP:** no data
Test substance: no data
Remark: Versuchsdurchführung in Anlehnung an den OECD-Confirmatory Test Stand 1976.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(50)

Type: aerobic
Inoculum: activated sludge
Concentration: 1000 mg/l related to Test substance
Degradation: 30 - 100 % after 14 day
Result: other
Method: other
Year: 1978 **GLP:**
Test substance:
Remark: 30 mg/l Activated Sludge
Method: Japanese Miti
Temperature: 25 deg C
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(55)

Type: aerobic
Inoculum: activated sludge
Concentration: 100 mg/l related to Test substance
Degradation: 30 - 100 % after 14 day
Result: other
Method: other
Year: 1978 **GLP:** no data
Test substance: other TS
Remark: 30 mg/l Activated Sludge
Method: Japanese Miti
Temp: 25 deg C pH 7.0
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(56)

Type: aerobic
Inoculum: activated sludge
Degradation: 72 %
Result: other
Method: other
Year: 1979 **GLP:** no data
Test substance: other TS
Remark: Method: Sturm
Results: % CO2 evolved
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(57)

Type: aerobic
Inoculum: activated sludge
Degradation: 82 %
Result: other
Method: other
Year: 1979 **GLP:** no data
Test substance: other TS
Remark: Method: OECD Screening test
Result: % DOC removal
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(57)

Type: aerobic
Inoculum: activated sludge
Degradation: 91 %
Result: other
Method: other
Year: 1979 **GLP:** no data
Test substance: other TS
Remark: Method: Sturm
Results: % DOC removal
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(57)

Type: aerobic
Inoculum: activated sludge
Degradation: 93 % after 4 day
Result: other
Method: other
Year: 1979 **GLP:**
Test substance:
Remark: Method: Zahn-Wellens
% DOC removal
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(57)

Type: aerobic
Inoculum: activated sludge
Degradation: 93 % after 4 day
Result: other
Method: other
Year: 1979 **GLP:** no data
Test substance: other TS
Remark: Method: Coupled units
Result: % DOC removal
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(57)

Type: aerobic
Inoculum: activated sludge
Result: other
Method: other
Year: 1979 **GLP:** no data
Test substance: other TS
Remark: Method: Closed bottle
Results: % BODT
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(57)

Type: aerobic
Inoculum: activated sludge
Concentration: 100 mg/l related to Test substance
Result: other
Method: other
Year: 1978 **GLP:** no data
Test substance: other TS
Remark: Degraded in 2 weeks
Temp: 25 deg C
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(58)

Type: aerobic
Inoculum: activated sludge, adapted
Concentration: 1000 mg/l related to COD (Chemical Oxygen Demand)
Degradation: 96 % after .6 day
Result: other
Method: other
Year: 1984 **GLP:**
Test substance:
Remark: Method: Warburg Respirometer
pH:7.0-7.2 Temperature: 30 deg C
Activated sludge acclimated using 1000 mg/l COD of Terephthatate in a SOAS unit for 24 days.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(59)

Type: aerobic
Inoculum:
Concentration: 20 mg/l related to Test substance
Degradation: 100 % after 2 day
Result: other
Method: other
Year: 1966 **GLP:** no data
Test substance: other TS
Remark: Soil inoculum from niagara silt loam
Medium: Soil and mineral salts
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(60)

Type: aerobic
Inoculum: other
Concentration: 40 mg/l related to Test substance
Degradation: 66 % after 28 day
Result: other
Method: other
Year: 1981 **GLP:** no data
Test substance: other TS
Remark: Method: French AFNOR
% Doc removal
Inoculum: 5 x 10 s germs/ml
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(57)

Type: aerobic
Inoculum: other
Concentration: 40 mg/l related to Test substance
Degradation: 66 % after 42 day
Result: other
Method: other
Year: 1981 **GLP:** no data
Test substance: other TS
Remark: Method: French AFNOR
% Doc removal
Inoculum: 5 x 10s germs/ml
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(57)

Type: aerobic
Inoculum: other
Result: other
Method: other
Year: 1978 **GLP:** no data
Test substance: other TS
Remark: Test param: Degredation in natural ecosystems
Method: Miti
Result: Confirmed to be significantly degraded
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(56)

Type: aerobic
Inoculum: other
Result: other
Method: other
Year: 1983 **GLP:** no data
Test substance: other TS
Remark: Inoculum: Soil bacteria
Results: decomposes in 2 days.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(61)

Type: aerobic
Inoculum: other
Concentration: 3000 mg/l related to Test substance
Result: other
Method: other
Year: 1977 **GLP:** no data
Test substance: other TS
Remark: Inoculum: Psendommas acidouorans
Results: degraded in 30 days
Medium: Mineral salts
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(62)

Type: aerobic
Inoculum: other
Result: other
Method: other
Year: 1976 **GLP:** no data
Test substance: other TS
Remark: microbes (various pure cultures including P Testosteroni) isolated by enrichment from soil, plant debris, fresh and brackish water and raw sewage.
Result: Degrades
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(63)

Type: aerobic
Inoculum: other
Result: other
Method: other
Year: 1981 **GLP:** no data
Test substance:
Remark: Method 1: Warburg Respirometer
Chem Dose 10 umol
Result Degraded after lag
Temp 30C
pH 7.5
Medium: Mixed culture of bacteria isolated from freshwater sediment
Comm: Mixed cultures of bacteria from freshwater sediment grew aerobically and anaerobically on test cmpd but not other phthalic acid isomers, different aerobic and anaerobic metabolic pathways.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(64)

Type: aerobic
Inoculum: Pseudomonas sp. (Bacteria)
Concentration: 2000 mg/l related to DOC (Dissolved Organic Carbon)
Method: other: Bestaetigung des Abbaus durch Nachweis von Metaboliten.
Year: **GLP:** no data
Test substance: no data
Remark: Aus Gartenerde mit selektiver Anreicherungsmethode isoliert und aerob auf o-Phthalat gewachsen. Pseudomonas spec. kann in waessrigem Medium TPA aerob als alleinige Energie- und Kohlenstoffquelle nutzen.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(65)

Type: aerobic
Inoculum: Pseudomonas sp. (Bacteria)
Concentration: 2000 mg/l related to DOC (Dissolved Organic Carbon)
Method: other: Bestätigung des Abbaus durch Nachweis von Metaboliten
Year: **GLP:** no data
Test substance: no data
Remark: Aus Gartenerde mit selektiver Anreicherungsmethode isoliert und aerob auf o-Phthalat gewachsen. Pseudomonas spec. kann in wässrigem Medium TPA aerob als alleinige Energie- und Kohlenstoffquelle nutzen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(65)

Type: aerobic
Inoculum: activated sludge, adapted
Concentration: 1000 mg/l related to COD (Chemical Oxygen Demand)
Degradation: > 95 % after 2 day
Method: other: CSB-Messung, pH 7.0 - 7.2
Year: **GLP:** no data
Test substance: no data
Remark: Nach 24 Tagen Adaption. Aerober Abau in waessrigem Medium.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(66)

Type: aerobic
Inoculum: activated sludge, adapted
Concentration: 1000 mg/l related to COD (Chemical Oxygen Demand)
Degradation: > 95 % after 2 day
Method: other: CSB-Messung; pH-Wert: 7.0 - 7.2
Year: **GLP:** no data
Test substance: no data
Remark: Nach 24 Tagen Adaption. Aerober Abau in wässrigem Medium.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(66)

Type: aerobic
Inoculum: activated sludge, non-adapted
Concentration: 100 mg/l related to Test substance
Method: other: MITI-Test
Year: **GLP:** no data
Test substance: no data
Remark: Die Versuchsdauer betrug vermutlich 14 Tage, ein Abbaugrad in waessrigem Medium wurde nicht angegeben, die Substanz jedoch als biologisch abbau eingestuft.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(47)

Type: aerobic
Inoculum: activated sludge, non-adapted
Concentration: 100 mg/l related to Test substance
Method: other: MITI-Test
Year: **GLP:** no data
Test substance: no data
Remark: Die Versuchsdauer betrug vermutlich 14 Tage, ein Abbaugrad in wässrigem Medium wurde nicht angegeben, die Substanz jedoch als biologisch abbaubar eingestuft.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(47)

Type: aerobic
Inoculum: other bacteria: Bakterien
Concentration: 3.3 mg/l related to Test substance
Method: other: O2-Aufnahme, pH = 8
Year: **GLP:** no data
Test substance: no data
Remark: Bakterien aus Meeresboden isoliert, koennen in waessrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle aerob wachsen.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(67)

Type: aerobic
Inoculum: other bacteria: Bakterien
Concentration: 3.3 mg/l related to Test substance
Method: other: O2-Aufnahme; pH-Wert: 8
Year: **GLP:** no data
Test substance: no data
Remark: Bakterien aus Meeresboden isoliert, koennen in wässrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle aerob wachsen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(67)

Type: aerobic
Inoculum: Nocardia sp. (Bacteria)
Concentration: 4000 mg/l related to Test substance
Degradation: ca. 100 % after 110 hour(s)
Method: other: Zunahme der Truebung bei 578 nm; pH = 7.2
Year: **GLP:** no data
Test substance: no data
Remark: Aus Boden durch Anreicherungsmethode mit Phtalsaeure isoliert.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(68)

Type: aerobic
Inoculum: Bacillus cirroflagellosus (Bacteria)
Concentration: related to Test substance
Method: other: Zunahme der Truebung gemessen bei 660 nm
Year: **GLP:** no data
Test substance: no data
Remark: Aus Gartenerde isoliert. Bacillus cirroflagellosus kann in waessrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle aerob wachsen. Einsatzkonzentration: 500 - 2000 mg/l
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(69)

Type: aerobic
Inoculum: other bacteria: Bacillus sp., adaptiert
Concentration: 2000 mg/l related to Test substance
Degradation: = 100 % after 1 day
Method: other: Zunahme der Truebung gemessen bei 660 nm
Year: **GLP:** no data
Test substance: no data
Remark: Aus Gartenerde isoliert.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(70)

Type: aerobic
Inoculum: Pseudomonas sp. (Bacteria)
Method: other: Zunahme der Truebung, gemessen bei 660 nm
Year: **GLP:** no data
Test substance: no data
Remark: Aus Gartenerde mit selektiver Anreicherungsmethode isoliert, kann mit TPA aerob und anaerob als alleiniger Energie- und Kohlenstoffquelle in waessrigem Medium wachsen.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(71)

Type: aerobic
Inoculum: Nocardia sp. (Bacteria)
Concentration: 4000 mg/l related to Test substance
Degradation: ca. 100 % after 110 hour(s)
Method: other: Zunahme der Trübung bei 578 nm; pH-Wert: 7.2
Year: **GLP:** no data
Test substance: no data
Remark: Aus Boden durch Anreicherungsmethode mit Phtalsäure isoliert.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(68)

Type: aerobic
Inoculum: Bacillus cirroflagellosus (Bacteria)
Concentration: related to Test substance
Method: other: Zunahme der Trübung gemessen bei 660 nm
Year: **GLP:** no data
Test substance: no data
Remark: Aus Gartenerde isoliert. Bacillus cirroflagellosus kann in wässrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle aerob wachsen. Einsatzkonzentration: 500 - 2000 mg/l
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(69)

Type: aerobic
Inoculum: other bacteria: Bacillus sp., adaptiert
Concentration: 2000 mg/l related to Test substance
Degradation: = 100 % after 1 day
Method: other: Zunahme der Trübung gemessen bei 660 nm
Year: **GLP:** no data
Test substance: no data
Remark: Aus Gartenerde isoliert.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(70)

Type: aerobic
Inoculum: Pseudomonas sp. (Bacteria)
Method: other: Zunahme der Trübung, gemessen bei 660 nm
Year: **GLP:** no data
Test substance: no data
Remark: Aus Gartenerde mit selektiver Anreicherungsmethode isoliert, kann mit TPA aerob und anaerob als alleiniger Energie- und Kohlenstoffquelle in wässrigem Medium wachsen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(71)

Type: aerobic
Inoculum: Alcaligenes sp. (Bacteria)
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Alicaligenes spec. mit Phthalsäure als Isolationsmedium aus Boden isoliert, kann in wässrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle wachsen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(72)

Type: aerobic
Inoculum: Alcaligenes sp. (Bacteria)
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Alcaligenes spec. aus Boden isoliert, kann in wässrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle wachsen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(73)

Type: aerobic
Inoculum: Arthrobacter sp. (Bacteria)
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Arthrobakter spec. mit iso-Phthalsaeure bzw. TPA als Isolationsmedium aus Boden isoliert, kann in wässrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle wachsen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(72)

Type: aerobic
Inoculum: Arthrobacter sp. (Bacteria)
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Arthrobakter spec. aus Boden isoliert kann in wässrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle wachsen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(73)

Type: aerobic
Inoculum: Arthrobacter terregens (Bacteria)
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Aus industriellem Abwasserteich mit TPA als Isolationsmedium isoliert. Arthrobakter terregens kann in wässrigem Medium TPA als alleinige Energie- und Kohlenstoffquelle nutzen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(74)

Type: aerobic
Inoculum: Arthrobacter terregens (Bacteria)
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Aus Gartenerde isoliert. Arthrobakter terregens kann in wässrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle aerob wachsen. Einsatzkonzentration: 500 bis 2000 mg/l
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(69)

Type: aerobic
Inoculum: Bacillus cirroflagellosus (Bacteria)
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Bacillus cirroflagellosus aus einem industriellen Abwasserteich mit TPA als Isolationsmedium isoliert, kann in wässrigem Medium TPA als alleinige Energie- und Kohlenstoffquelle nutzen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(74)

Type: aerobic
Inoculum: Nocardia resticta (Bacteria)
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Nocardia restricta aus einem industriellen Abwasserteich mit TPA als Isolationsmedium isoliert, kann in wässrigem Medium TPA als alleinige Energie- und Kohlenstoffquelle nutzen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(74)

Type: aerobic
Inoculum: Nocardia resticta (Bacteria)
Concentration: related to Test substance
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Aus Gartenerde isoliert. Nocardia resticta kann in wässrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle aerob wachsen. Einsatzkonzentration: 500 - 2000 mg/l
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(69)

Type: aerobic
Inoculum: Pseudomonas alcaligenes (Bacteria)
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Aus industriellem Abwasserteich mit TPA als Isolationsmedium isoliert; Pseudomonas alcaligenes kann TPA in wässrigem Medium als alleinige Energie- und Kohlenstoffquelle nutzen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(74)

Type: aerobic
Inoculum: Pseudomonas alcaligenes (Bacteria)
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Aus Gartenerde isoliert. Pseudomonas alcaligenes kann in wässrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle aerob wachsen. Einsatzkonzentration: 500 - 2000 mg/l
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(69)

Type: aerobic
Inoculum: Pseudomonas sp. (Bacteria)
Concentration: 200 mg/l related to Test substance
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Abbaugrad nach 14 h: 100 % in wässrigem Medium; Aus Belebtschlamm einer industriellen Kläranlage isoliert; Aerober Abbau
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(75)

Type: aerobic
Inoculum: Pseudomonas sp. (Bacteria)
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Aus Boden isoliert; aerober Abbau in wässrigem Medium; kann TPA als alleinige Energie- und Kohlenstoffquelle nutzen
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(76)

Type: aerobic
Inoculum: Pseudomonas testosteroni (Bacteria)
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Pseudomonas testoteroni mit o-Phthalate als alleiniger Kohlenstoffquelle isoliert, kann aerob in wässrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle wachsen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(77)

Type: aerobic
Inoculum: other bacteria: Acinetobakter sp.
Concentration: 200 mg/l related to Test substance
Degradation: ca. 100 %
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(75)

Type: aerobic
Inoculum: other bacteria: Mycobakter lacticolum
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Mycobakter lacticolum aus Belebtschlamm einer industriellen Kläranlage isoliert, kann in wässrigem Medium TPA aerob abbauen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(78)

Type: aerobic
Inoculum: Alcaligenes sp. (Bacteria)
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Alicaligenes spc. mit Phthalsaeure als Isolationsmedium aus Boden isoliert, kann in waessrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle wachsen.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(72)

Type: aerobic
Inoculum: Alcaligenes sp. (Bacteria)
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Alcaligenes spec. aus Boden isoliert, kann in waessrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle wachsen.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(73)

Type: aerobic
Inoculum: Arthrobacter sp. (Bacteria)
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Arthrobakter spec. mit iso-Phthalsaeure bzw. TPA als Isolationsmedium aus Boden isoliert, kann in waessrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle wachsen.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(72)

Type: aerobic
Inoculum: Arthrobacter sp. (Bacteria)
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Arthrobakter spec. aus Boden isoliert kann in waessrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle wachsen.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(73)

Type: aerobic
Inoculum: Arthrobacter terregens (Bacteria)
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Aus industriellem Abwasserteich mit TPA als Isolationsmedium isoliert. Arthrobakter terregens kann in waessrigem Medium TPA als alleinige Energie- und Kohlenstoffquelle nutzen.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(74)

Type: aerobic
Inoculum: Arthrobacter terregens (Bacteria)
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Aus Gartenerde isoliert. Arthrobakter terregens kann in waessrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle aerob wachsen. Einsatzkonzentration: 500 - 2000 mg/l
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(69)

Type: aerobic
Inoculum: Bacillus cirroflagellosus (Bacteria)
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Bacillus cirroflagellosus aus einem industriellen Abwasserteich mit TPA als Isolationsmedium isoliert, kann in waessrigem Medium TPA als alleinige Energie- und Kohlenstoffquelle nutzen.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(74)

Type: aerobic
Inoculum: Nocardia resticta (Bacteria)
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Nocardia restricta aus einem industriellen Abwasserteich mit TPA als Isolationsmedium isoliert, kann in waessrigem Medium TPA als alleinige Energie- und Kohlenstoffquelle nutzen.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(74)

Type: aerobic
Inoculum: Nocardia resticta (Bacteria)
Concentration: related to Test substance
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Aus Gartenerde isoliert. Nocardia resticta kann in waessrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle aerob wachsen. Einsatzkonzentration: 500 - 2000 mg/l
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(69)

Type: aerobic
Inoculum: Pseudomonas alcaligenes (Bacteria)
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Aus industriellem Abwasserteich mit TPA als Isolationsmedium isoliert; Pseudomonas alcaligenes kann TPA in waessrigem Medium als alleinige Energie- und Kohlenstoffquelle nutzen.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(74)

Type: aerobic
Inoculum: Pseudomonas alcaligenes (Bacteria)
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Aus Gartenerde isoliert. Pseudomonas alcaligenes kann in waessrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle aerob wachsen. Einsatzkonzentration: 500 - 2000 mg/l
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(69)

Type: aerobic
Inoculum: Pseudomonas sp. (Bacteria)
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Aus Boden isoliert; aerober Abbau in waessrigem Medium; kann TPA als alleinige Energie- und Kohlenstoffquelle nutzen
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(76)

Type: aerobic
Inoculum: Pseudomonas testosteroni (Bacteria)
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Pseudomonas testoteroni mit o-Phthalate als alleiniger Kohlenstoffquelle isoliert, kann aerob in waessrigem Medium mit TPA als alleiniger Energie- und Kohlenstoffquelle wachsen.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(77)

Type: aerobic
Inoculum: other bacteria: Acinetobakter sp.
Concentration: 200 mg/l related to Test substance
Degradation: ca. 100 %
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(75)

Type: aerobic
Inoculum: other bacteria: Mycobakter lacticolum
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Mycobakter lacticolum aus Belebtschlamm einer industriellen Klaeranlage isoliert, kann in waessrigem Medium TPA aerob abbauen.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(78)

Type: aerobic
Inoculum: Pseudomonas sp. (Bacteria)
Concentration: 200 mg/l related to Test substance
Method: other: keine Daten
other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Abbaugrad nach 14 h: 100 % in waessrigem Medium; Aus Belebtschlamm einer industriellen Klaeranlage isoliert; Aerober Abbau
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(75)

Type: anaerobic
Inoculum: other
Result: other
Method: other
Year: 1981 **GLP:** no data
Test substance:
Remark: Method 1: Warburg respirometer
Chem Dose 10 umol
Result Rapid degradation
Temp 30c
pH 7.5
Medium 1: Mixed culture of bacteria isolated from freshwater sediment.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(79)

Type:
Inoculum: activated sludge, non-adapted
Degradation: = 0 % after 14 day
Method: other: ORIGINAL-MITI-Test, Biodegradability and Bioaccumulation Testof Chemical Substances (C-5/98/JAP) 1978
Year: **GLP:** no data
Test substance: no data
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(50)

Type:
Inoculum: activated sludge, non-adapted
Degradation: = 0 % after 14 day
Method: other: ORIGINAL-MITI-Test, Biodegradability and Bioaccumulation Test of Chemical Substances (C-5/98/JAP) 1978
Year: **GLP:** no data
Test substance: no data
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(50)

Type:
Inoculum:
Method:
Year: **GLP:**
Test substance:
Remark: In a modified OECD screening test for biodegradability a Dissolved Organic carbon (DOC) value of 82% was obtained using a test concentration of 10 or 20 mg/l, a 19-day test period, and 0.05% effluent solution. In a "Coupled Units OECD test" where 2.5 g/l of dry matter od sludge was taken from a communal sludge treatment plant, a 1-day DOC value of 93 + 3% was recorded for a terephthalic acid concetration of at least 12 mg/l [not further specified] (Gerike & Fischer, 1979).
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Type:
Inoculum:
Method:
Year: **GLP:**
Test substance:
Remark: materiale facilmente biodegradabile (BOD20>60%)
Source: SIPET SpA Patrica (FR)

3.6 BOD5, COD or BOD5/COD Ratio

Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

3.7 Bioaccumulation

Species:
Exposure period:
Concentration:
BCF:
Elimination:
Method: other
Year: 1988 **GLP:** no data
Test substance:
Remark: Result: Log BCF = 1.29 calculated.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

Species:
Exposure period:
Concentration:
BCF:
Elimination:
Method:
Year: **GLP:**
Test substance:
Remark: Il logaritmo del coefficiente di ripartizione ottanolo/acquaè 1.25. Non si prevede che il materiale causi effetti negativi a lungo termine sull'ambiente acquatico (log Pow<3)
Source: SIPET SpA Patrica (FR)

3.8 Additional Remarks

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AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: semistatic
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC0: = 500
LC50: 798 - 1640
LC100: = 1500
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1991 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Mean value 1157 mg/l
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(80)

Type: semistatic
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC0: = 500
LC50: = 1157
LC100: = 1500
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: Nominal concentration. Solvent DMSO (0.05 -0.3% v/v) added.
Source: INCA INTERNATIONAL S.p.A. Milan

(81)

Type: semistatic
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:**
LC0: = 500
LC50: = 1157
LC100: = 1500
Method: other: Semistatischer Test
Year: **GLP:** no data
Test substance: no data
Remark: Nominalkonzentration; geprüft wurde in drei Konzentrationen (500, 1000, 1500 mg/l) in Gegenwart von Dimethylsulfoxid (0.05 - 0.3 % (v/v)) als Lösungsvermittler. Bei der Lösung mit der höchsten geprüften Konzentration wurde während des Versuches Trübung und Substanzausfällung beobachtet.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(82)

Type: static
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC0: > 500
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1989 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Nominalkonzentration. Geprueft wurde nur bei einer Konzentration (500 mg/l) in Gegenwart von TWEEN 80 (0.095 ml/l) als Loesungsvermittler. Die pH-Werte lagen zwischen 8.0 am Versuchsbeginn (eingestellt mit Natronlauge) und 5.0 am Versuchsende. Es waren nach 72 h Substanzablagerungen am Beckenboden zu beobachten. Analytisch (HPLC-UV) wurde eine Istkonzentration von 19 mg/l ermittelt.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire

(83)

Type: static
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC0: > 500
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1989 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Nominalkonzentration. Geprüft wurde nur bei einer Konzentration (500 mg/l) in Gegenwart von TWEEN 80 (0.095 ml/l) als Lösungsvermittler. Die pH-Werte lagen zwischen 8.0 am Versuchsbeginn (eingestellt mit Natronlauge) und 5.0 am Versuchsende. Es waren nach 72 h Substanzablagerungen am Beckenboden zu beobachten. Analytisch (HPLC-UV) wurde eine Istkonzentration von 19 mg/l ermittelt.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(84)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: > 1000
LC0: > 922
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1992 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Dose / exposure levels: Nominal concentrations of 130, 220, 350, 600 and 1000 mg/l

The 96 hour LC0 was determined to be >=922 mg/l (measured concentration) of terephthalic acid and terephthalic sodium salt.

The nominal No Observed Effect Concentration (96 hour NOEC) was >=1000mg/l.

Under the test conditions it was believed that some of the terephthalic acid hydrolysed to a terephthalic sodium salt.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(52)

Type:
Species: Oncorhynchus mykiss (Fish, fresh water)
Exposure period:
Unit: mg/l **Analytical monitoring:**
LC50: = 1157
Method:
Year: **GLP:**
Test substance:
Source: SIPET SpA Patrica (FR)

4.2 Acute Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC50: > 982
Method: OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year: 1992 **GLP:** yes
Test substance: other TS
Remark: Based on measured average concentrations, the 48 hour EC0 was 520.2mg/l TPA and Terephthalic sodium salt. Based on measured concentrations, the 48 hour EC50 was > 982mg/l. It is believed that some of the TPA hydrolized under test conditions to Terephthalic sodium salts.
Source: INCA INTERNATIONAL S.p.A. Milan
Test substance: TPA, no indication about purity.

(85)

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** yes
EC0: = 520.2
EC50: > 982
Method: OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year: 1991 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Under the test conditions it was believed that some of the terephthalic acid hydrolysed to a terephthalic sodium salt.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(52)

Species: Daphnia magna (Crustacea)
Exposure period:
Unit: mg/l **Analytical monitoring:**
EC50: = 409
Method:
Year: **GLP:**
Test substance:
Source: SIPET SpA Patrica (FR)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus subspicatus (Algae)
Endpoint: growth rate
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
NOEC: >= 409
Method: OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year: 1992 **GLP:** yes
Test substance: other TS
Remark: The NOEC based on nominal concentrations was >= 1000mg/l. The NOEC based on measured average concentrations was >= 409mg/l. Under test conditions, it is believed that some of the TPA hydrolized to Terephthalic sodium salt.
Source: INCA INTERNATIONAL S.p.A. Milan
Test substance: TPA, no indication about purity.

(85)

Species: Scenedesmus subspicatus (Algae)
Endpoint: growth rate
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: >= 1000
Method: OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year: 1992 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Dose / exposure levels: Nominal concentrations of 62.5, 125, 250, 500and 1000 mg/l

The nominal No Observed Effect Concentration (96 hour NOEC) was >= 1000mg/l.
The NOEC based upon measured average concentrations was >= 409 mg/l.
Under the test conditions it was believed that some of the terephthalic acid hydrolysed to a terephthalic sodium salt.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(52)

Species: Scenedesmus subspicatus (Algae)
Endpoint:
Exposure period:
Unit: mg/l **Analytical monitoring:**
EC0: > 982
Method:
Year: **GLP:**
Test substance:
Remark: No observed effect Concentration (NOEC)
Source: SIPET SpA Patrica (FR)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: activated sludge of a predominantly domestic sewage
Exposure period: 16 day
Unit: mg/l **Analytical monitoring:** yes
EC50: = 1392.8
Method: OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year: 1991 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: The respiration rate of activated sludge was not inhibited at saturated concentrations during the range finding test.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(52)

Type: field
Species: domestic sewage
Exposure period: 16 day
Unit: mg/l **Analytical monitoring:** no data
EC50: = 1392.8
Method: OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year: 1992 **GLP:** yes
Test substance: other TS
Remark: The respiration rate of activated sludge was not inhibited at saturated concentrations during the range finding test.
Source: INCA INTERNATIONAL S.p.A. Milan
Test substance: TPA, no indication about purity.

(86)

Type: other: keine Angaben
Species: activated sludge
Exposure period:
Unit: mg/l **Analytical monitoring:** no data
EC50: = 1392.8
EC5 : = 650.6
NOEC : = 500
Method: OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Keine Angaben zur Expositionszeit.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(87)

Type: other: keine Angaben
Species: other protozoa: Fasciola hepatica (Grosser Leberegel)
Exposure period: 2 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC0: = 830
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Testparameter: Beweglichkeit, Verfärbung
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(88)

Type: other: keine Angaben
Species: other protozoa: Tetrahymena pyriformis (Wimpertierchen)
Exposure period: 24 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC50: = 800
Method: other: Vermehrungshemmtest
Year: **GLP:** no data
Test substance: no data
Remark: DMSO als Lösungsvermittler
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(89)

Type:
Species: other protozoa: Fasciola hepatica (Grosser Leberegel)
Exposure period: 2 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC0: = 830
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Testparameter: Beweglichkeit, Verfaerbung
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(88)

Type:
Species: other protozoa: Tetrahymena pyriformis (Wimpertierchen)
Exposure period: 24 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC50: = 800
Method: other: Vermehrungshemmtest
Year: **GLP:** no data
Test substance: no data
Remark: DMSO als Loesungsvermittler
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(89)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

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4.5.2 Chronic Toxicity to Aquatic Invertebrates

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TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

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4.6.2 Toxicity to Terrestrial Plants

Species: Avena sativa (Monocotyledon)
Endpoint: other: Laengenwachstum
Expos. period: 1 day
Unit: mg/l
EC0 : = 100
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Nominalkonzentration
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(90)

Species: Oryza sativa (Monocotyledon)
Endpoint: other: Laengenwachstum
Expos. period: 5 day
Unit: mg/l
EC0 : > 10
EC20 : = 100
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Nominalkonzentration
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(90)

Species: Avena sativa (Monocotyledon)
Endpoint: other: Längenwachstum
Expos. period: 1 day
Unit: mg/l
EC0 : = 100
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Nominalkonzentration
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(90)

Species: Oryza sativa (Monocotyledon)
Endpoint: other: Längenwachstum
Expos. period: 5 day
Unit: mg/l
EC0 : > 10
EC20 : = 100
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Nominalkonzentration
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(90)

4.6.3 Toxicity to other Non–Mamm. Terrestrial Species

Species: Drosophila melanogaster (arthropod (Diptera))
Endpoint: mortality
Expos. period: 3 day
Unit: mg/kg bw
LC0: = 166
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Larven und Puppen
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(91)

Species: Drosophila melanogaster (arthropod (Diptera))
Endpoint: mortality
Expos. period: 3 day
Unit: mg/kg bw
LC0: = 166
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Larven und Puppen
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire

(91)

Species: other
Endpoint: weight
Expos. period:
Unit:
Method: other
Year: **GLP:** no data
Test substance: other TS
Remark: Groups of 15 chickens wew given diets containing 0.4% TPA with and Without added stilbestrol.

Test results: "TPA increased body weight slightly, but significantly increased fat weight. No clear changes in the testes or comb weights were seen. Simultaneous administration of TPA and stilbestrol delayed growth, and body fat decreased. Stilbestrol doses > 0.1% atrophied the testes and comb
Source: INCA INTERNATIONAL S.p.A. Milan
Test substance: TPA, no indication about purity.

(92)

Species: other: Weiße Leghorn-Hühner
Endpoint:
Expos. period:
Unit: other: mg/Tier/Tag
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Keine Wirkung auf die Legeleistung und Eierqualität.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(93)

Species: other: Weisse Leghorn-Huehner
Endpoint:
Expos. period:
Unit: other: mg/Tier/Tag
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Keine Wirkung auf die Legeleistung und Eierqualitaet.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire

(93)

4.7 Biological Effects Monitoring

–

4.8 Biotransformation and Kinetics

–

4.9 Additional Remarks

–

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: = 18800 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: other TS
Source: INCA INTERNATIONAL S.p.A. Milan
Test substance: TPA, no indication about purity.

(94)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: = 15380 mg/kg bw
Method:
Year: **GLP:**
Test substance:
Source: SIPET SpA Patrica (FR)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: > 15380 mg/kg bw
Method: other
Year: 1975 **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Remark: Five male and five female rats tested per group.
Doses employed were - 6834, 10250 and 15380 mg/kg.

One test animal died. Toxic signs in the other test animals included transitory CNS depression and diarrhoea. No gross pathologic alterations were observed.

Note - The performing laboratory had problems with the accuracy of some of their data at this time. Consequently the data should not be given equal weighting compared to other studies.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(95)

5. Toxicity

date: 22-FEB-2000
Substance ID: 100-21-0

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: > 5000 mg/kg bw
Method: other
Year: 1990 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: 5 rats per group.
Parameters Monitored during the study - Gross Necroscopy, Mortality, Behaviour
12 day post exposure observation period.

Terephthalic acid was prepare as a 50% (w/v) aqueous suspension in reverse osmosis purified water. No deaths occurred. Gross necroscopy findings were within normal limits in all rats. No clinical signs were noted in the animals except for slight fur staining in one rat and redness around the nose in another.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(96)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: > 6400 mg/kg bw
Method:
Year: 1963 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(97)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: 1960 mg/kg bw
Method:
Year: 1966 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(98)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: 18800 mg/kg bw
Method:
Year: 1972 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(99)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: > 5000 mg/kg bw
Method:
Year: 1966 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(100)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: = 18800 mg/kg bw
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(101)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: > 5000 mg/kg bw
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Geschlecht: männlich
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(102)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: = 1960 mg/kg bw
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Geschlecht: weiblich
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(103)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Value: 5000 mg/kg bw
Method:
Year: 1968 **GLP:**
Test substance:
Remark: Mice that died did so 8-48 hr after administration. The only symptom of toxicity was lethargy.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(104)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Value: 6400 mg/kg bw
Method:
Year: 1975 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(105)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Value: 1470 mg/kg bw
Method:
Year: 1966 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(98)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Value: > 5000 mg/kg bw
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(102)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Value: = 6400 mg/kg bw
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(106)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Value: = 1470 mg/kg bw
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Geschlecht: weiblich
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(103)

Type: LDLo
Species: mouse
Sex:
Number of Animals:
Vehicle:
Value: 10000 mg/kg bw
Method:
Year: 1982 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(107)

Type: LDLo
Species: mouse
Sex:
Number of Animals:
Vehicle:
Value: = 10000 mg/kg bw
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(108)

Type: other
Species: mouse
Sex:
Number of Animals:
Vehicle:
Value:
Method:
Year: 1965 **GLP:** no data
Test substance: no data
Remark: 10 gm/kg:
distributed movement coordination, damaged gi tract, caused fluid retention, and tissue death in internal organs. 40% of treated animals died within 6-12 days.

5 gm/kg:
pronounced "vascular" disorders, effects on nervous system function and a reduced rate.

0.5 gm/kg:
only mild transient effects on the nervous system - excitation and depression.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(109)

Type:
Species:
Sex:
Number of Animals:
Vehicle:
Value:
Method:
Year: **GLP:**
Test substance:
Remark: NON-HUMAN.-
Groups of 10 male and 10 female rats of two different strains were maintained on diets containing 0, 0.03, 0.125, 0.5, 0,2 and 5.0 % terephthalic acid for 90 days prior to mating. The fertility, litter size and foetal malformation rate was unaffected. The survival of the pups (at day 1 or 21) was reduced in the groups receiving 2 or 5% âbout 1000 and 2500 mg/kg bw/day respectively]. Indications of range,

weight gain being markedly reduced at 2 and 5%. An increased number of adult deaths also occurred within the top dose group (CIIT; 1982).
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value: > 999999 mg/l
Method:
Year: **GLP:**
Test substance:
Remark: Vapour formation is improbable because the phisical properties
Source: SIPET SpA Patrica (FR)

Type: LC50
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 2 hour(s)
Value: > 2.02 mg/l
Method: other
Year: 1987 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: No rats died during the study. Gross Necroscopy findings were within normal limits in seven rats. One male rat had dark lungs and one male and female rat had enlarged mandibular lymph nodes.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (110)

Type: LC50
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 2 hour(s)
Value: > 2.02 mg/l
Method: other
Year: 1987 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: No deaths after a 2 hour exposure. Some rats had diarrhoea, redness around the nose and hair loss. At post mortem one rat had dark lungs and two had enlarged mandibular lymph nodes.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(111)

Type: other
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 30 minute(s)
Value:
Method:
Year: 1988 **GLP:** no data
Test substance: other TS
Remark: Dose levels of 100, 200 and 400 mg/m3. No adverse effects on pulmonary function, bronchoalveolar lavage parameters or histopathology. Reversible, dose-related rhinorrhaea. Mild irritant to nucous membranes.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
Test substance: Pyrotechemicaly disseminated TA

(112)

Type: other
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value:
Method: other
Year: 1987 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Groups of 10 male rats were each exposed nose only for a single four hour period to aerosols of terphthalic acid at target concentrations of 30, 100 or 1000 mg/m3.

No treatment related abnormalities were observed.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(113)

Type: other
Species: mouse
Sex:
Number of Animals:
Vehicle:
Exposure time: 10 minute(s)
Value: 1 mg/l
Method: other
Year: 1987 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Groups of 5 male mice were each exposed, nose only, for a single 10 minute period to aerosols of terephthalic acid at target concentrations of 1000 mg/m3. Their respiratory rate was measured using optical plethysmography, before, during and after exposure.

A mean rate of depression of 19% was measured indicating that terephthalic acid has a low irritant potential.

Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (113)

Type:
Species:
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value:
Method:
Year: **GLP:**
Test substance:
Remark: An abstract notes that male rats and male quinea-pigs exposed 6 hr/day, 5 day/wk, for 6 months to terephthalic acid dust levels of 10 mg/m3 (respirable dust concentration 5 mg/m3) suffered no effects on body weight, organ weights, clinical chemistry, or tissue structure (Lewis et a1. 1982). An English abstract of a Russian paper states that in rats, daily 2-hr exposures, 6 day/wk of 2-5 mg/m3 produced effects on the vascular, respiratory and nervous systems [not further described] (Sanina, 1965).
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rabbit
Sex:
Number of Animals:
Vehicle:
Value: > 2000
Method: OECD Guide-line 402 "Acute dermal Toxicity"
Year: 1990 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Five male and 5 female rabbits were given an occluded dose of 2000mg/kg which was left in place for 14 days. No deaths occurred. Mild dermal irritation was observed within the application site of 6 rabbits immediately following unwrapping.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (114)

Type:
Species:
Sex:
Number of
Animals:
Vehicle:
Value:
Method:
Year: GLP:
Test substance:
Remark: Not detected
Source: SIPET SpA Patrica (FR)

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: rat
Sex:
Number of
Animals:
Vehicle:
Route of admin.: i.p.
Value: 2250 mg/kg bw
Method:
Year: GLP:
Test substance:
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(100)

Type: LD50
Species: rat
Sex:
Number of
Animals:
Vehicle:
Route of admin.: i.p.
Value: 1210 mg/kg bw
Method:
Year: 1966 GLP: no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(98)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 2250 mg/kg bw
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Geschlecht: männlich
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(102)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 1210 mg/kg bw
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Geschlecht: weiblich
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(103)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: 880 mg/kg bw
Method:
Year: 1966 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(98)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: 1430 mg/kg bw
Method:
Year: 1968 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(104)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: 1900 mg/kg bw
Method:
Year: **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(115)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 1430 mg/kg bw
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(116)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 880 mg/kg bw
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Geschlecht: weiblich
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(103)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 1900 mg/kg bw
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Geschlecht: männlich
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(117)

Type: LD100
Species: rat
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: 3500 mg/kg bw
Method:
Year: 1964 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(118)

Type: LD100
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: 3200 mg/kg bw
Method:
Year: 1971 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(115)

Type: other
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: 2000 mg/kg bw
Method:
Year: 1958 **GLP:** no data
Test substance: no data
Remark: Main toxic symptoms were convulsions.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(119)

Type: other
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: 300 mg/kg bw
Method:
Year: **GLP:**
Test substance:
Remark: Reduced kidney function - retention of phenolsulphophthalein.
Not seen in mice administrated 100 mg/kg.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(104)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.v.
Value: 770 mg/kg bw
Method:
Year: 1966 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(98)

5. Toxicity

date: 22-FEB-2000
Substance ID: 100-21-0

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.v.
Value: = 770 mg/kg bw
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Geschlecht: weiblich
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(103)

Type: LD100
Species: dog
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.v.
Value: 769 mg/kg bw
Method:
Year: 1971 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(115)

Type:
Species:
Sex:
Number of Animals:
Vehicle:
Route of admin.:
Value:
Method:
Year: **GLP:**
Test substance:
Remark: Other local effects.-
Non-human. An English abstract of a Russian paper notes that five daily 2-hr esposures to atmospheric concentrations of 2-5 mg/m3 produced mucous menbrane redness in rats. An increase in respiration rate was also recorderd (such an increase is normally taken as an indication of respiratory tract irritation) (Sanina, 1965).
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.: not irritating
Method: other
Year: **GLP:** no data
Test substance: other TS
Remark: Test method: FHSA test (0.4/8.0)
Source: INCA INTERNATIONAL S.p.A. Milan
Test substance: TPA, no indication about purity.

(120)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: slightly irritating
EC classificat.: not irritating
Method:
Year: **GLP:**
Test substance:
Remark: PDIS of 02/8.0
Source: SIPET SpA Patrica (FR)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.: not irritating
Method:
Year: 1990 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Three males rabbits were given a dermal dose of 0.5g terephthalic acid for 72 hours. The application sites were rinsed with 2ml of 0.9% saline. No irritancy or corrosivity was observed.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(121)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: slightly irritating
EC classificat.: not irritating
Method:
Year: 1975 **GLP:** no
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(122)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: slightly irritating
EC classificat.:
Method:
Year: 1981 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(123)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: slightly irritating
EC classificat.:
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(124)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.:
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Einwirkzeit: 24 h
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(106)

Species: rat
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.:
Method:
Year: 1975 **GLP:** no data
Test substance: no data
Remark: 80 mg in 0.2 ml aqueous solution for 24 hrs. Applied 5 times in 10 days.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(125)

Species: rat
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result:
EC classificat.:
Method:
Year: 1965 **GLP:** no data
Test substance: no data
Remark: Exposure to atmospheres containing 2-5 mg/m3 produced skin redness.
Skin erosions induced by 14-20 daily exposures.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(126)

Species:
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result:
EC classificat.:
Method:
Year: GLP:
Test substance:
Remark: Human.-
A standard text describes terephthalic acid as a mild irritant [presumably in man], but provides no support for this statement (Merck, 1983).
Non-human.-
In the rat, a suspension (80 mg in 0,2 ml of a weak aqueous detergent solution) in (semi-occluded) contact with the skin for 48 hr, applied five times in 10 days, was not irritating (Moffitt et al. 1975).
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: not irritating
EC classificat.: not irritating
Method: other
Year: GLP: no data
Test substance: other TS
Remark: Test method: FHSA test (14.0/110.0).
Source: INCA INTERNATIONAL S.p.A. Milan
Test substance: TPA, no indication about purity.

(120)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: slightly irritating
EC classificat.:
Method:
Year: GLP:
Test substance:
Remark: Primary eye irritation score of 10/110

Source: SIPET SpA Patrica (FR)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: not irritating
EC classificat.: not irritating
Method: other
Year: 1990 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Three male rabbits were given 0.1g terephthalic acid in the eye. No irritancy was observed
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(127)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: slightly irritating
EC classificat.: not irritating
Method: other
Year: 1975 **GLP:** no
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(128)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: slightly irritating
EC classificat.:
Method:
Year: 1975 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(125)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: slightly irritating
EC classificat.:
Method:
Year: 1972 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(129)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: slightly irritating
EC classificat.:
Method:
Year: 1986 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(130)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: slightly irritating
EC classificat.:
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Einwirkzeit nicht angegeben
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(106)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: slightly irritating
EC classificat.:
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Dosierung: 500 mg; Einwirkzeit: 24 h
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(131)

Species:
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result:
EC classificat.:
Method:
Year: **GLP:**
Test substance:
Remark: Non-human.-
A brief citation of a Russian study notes that a 500 mg dose caused moderate eye irritation in rabbits (marhold, 1972). Small doses [not further describ ed] aoolied to the eye of rabbits were slightly irritating to the conjunctiva, but evidently caused no corneal damage (Eastman).
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

5.3 Sensitization

Type: other
Species: guinea pig
Number of Animals:
Vehicle:
Result: not sensitizing
Classification: not sensitizing
Method: other
Year: **GLP:** no data
Test substance: other TS
Remark: Test method: "TPA was applied as a 50% paste in 1% aqueous duponol to the intact skin of Guinea Pigs."
Source: INCA INTERNATIONAL S.p.A. Milan
Test substance: TPA, no indication about purity.

(132)

Type:
Species:
Number of Animals:
Vehicle:
Result: not sensitizing
Classification:
Method: other: keine Angaben
Year: GLP: no data
Test substance: no data
Remark: Keine näheren Angaben
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(106)

Type:
Species:
Number of Animals:
Vehicle:
Result: not sensitizing
Classification:
Method:
Year: 1975 GLP: no data
Test substance: no data
Remark: No further data available.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(105)

5.4 Repeated Dose Toxicity

Species: rat Sex: male
Strain:
Route of admin.: inhalation
Exposure period: 28 days
Frequency of treatment: 6 hours per day, 5 days per week for 4 weeks
Post. obs. period:
Doses: 0.0215 mg/l
Control Group:
NOAEL: .0215 mg/l
Method: other
Year: 1973 GLP: no
Test substance: no data
Result: No deaths were recorded and no signs of toxicity or gross pathological changes were noted.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(133)

Species: rat **Sex:** male/female
Strain:
Route of admin.: inhalation
Exposure period: 28 days
Frequency of treatment: 6 hours per day for 4 weeks
Post. obs. period: 3 days
Doses: 0, 0.52, 1.2, 3.3 mg/m3
Control Group: yes, concurrent no treatment
NOAEL: .003 mg/l
Method:
Year: **GLP:** yes
Test substance: no data
Result: No adverse effects of any kind were observed during the study or at necroscopy.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(134)

Species: rat **Sex:** male
Strain:
Route of admin.: inhalation
Exposure period: 25 days
Frequency of treatment: 6 hours per day, 7 days per week
Post. obs. period: 28 days
Doses: 10 mg/m3
Control Group: no data specified
Method: other
Year: 1989 **GLP:** yes
Test substance: no data
Remark: Pharmacokinetic study.
Parameters Monitored during the study - Body weight, Gross Necroscopy, Mortality, Observed for a four week recovery period. Blood and urine samples were collected one day prior to exposure and after 1, 5, 10, 15, 25 days of exposure and every 7 days during the 28 day recovery period.
Result: The highest blood concentration was 2.7ug/ml after 25 days exposure. No deaths or clinical signs were seen.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(135)

date: 22-FEB-2000

5. Toxicity Substance ID: 100-21-0

Species: rat **Sex:** male/female
Strain:
Route of admin.: inhalation
Exposure period: 25 days
Frequency of treatment: 6 hours per day, 7 days per week
Post. obs. period: 0 days
Doses: 10 mg/m3
Control Group: no data specified
Method: other
Year: 1989 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Pharmacokinetic study.
Parameters Monitored during the study - Body weight, Gross Necroscopy, Mortality, Observed for a four week recovery period. Blood and urine samples were collected one day prior to exposure and after 1, 5, 10, 15, 25 days of exposure and every 7 days during the 28 day recovery period.
Result: The highest blood concentration was 2.7ug/ml after 25 days exposure. No deaths or clinical signs were seen.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(135)

Species: rat **Sex:** no data
Strain:
Route of admin.: inhalation
Exposure period: 4 weeks
Frequency of treatment: 6 hr/day, 5 days/week
Post. obs. period:
Doses: 25 mg/m3
Control Group: no data specified
Method:
Year: 1982 **GLP:** no data
Test substance: no data
Remark: No effects of toxicological relevance.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(136)

date: 22-FEB-2000
5. Toxicity Substance ID: 100-21-0

Species: rat **Sex:** male/female
Strain:
Route of admin.: inhalation
Exposure period: 4 weeks
Frequency of treatment: 6 hr/day, 5 days/week
Post. obs. period:
Doses: 0.52, 1.19, 3.31 mg/m3
Control Group: yes, concurrent no treatment
Method:
Year: 1988 **GLP:** no data
Test substance: other TS
Remark: No deaths or overt chemical signs reported.
No effects of TA exposure noted at necropsy
No significant changes in body or organ weights, haematology or clinical chemistry parameters.

Minimal degeneration of the tracheal epithelium in 19/20 of the 3.31 mg/m3 group and 1/20 of the controls.

Assessment of pulmonary air flow, transpulmonary pressure, tidal volume, dynamic lung complaince, airway resistance, respiratory rate and minute volume showed no differences between the controls and 3.31 mg/m3 groups.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
Test substance: Resipirable TA dust

(137)

Species: rat **Sex:** male
Strain: Sprague-Dawley
Route of admin.: inhalation
Exposure period: 6 months
Frequency of treatment: 6 hr/day, 5 days/week
Post. obs. period:
Doses: 10 mg/m3
Control Group: yes, concurrent no treatment
Method:
Year: 1982 **GLP:** no data
Test substance: no data
Remark: 10 mg/m3 - "respirable" dust concn = 5 mg/m3

No effects on body weights, organ (lung, liver, kidney, spleen) weights, clinical chemistry or tissue structure.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(138) (139)

Species: rat **Sex:** no data
Strain:
Route of admin.: inhalation
Exposure period: no data
Frequency of treatment: 2 hr/day, 6 days/week
Post. obs. period:
Doses: 2 - 5 mg/m3
Control Group: no data specified
Method:
Year: 1965 **GLP:** no data
Test substance: no data
Remark: effects on the vascular, respiratory and nervous systems.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(140)

Species: rat **Sex:** no data
Strain:
Route of admin.: inhalation
Exposure period:
Frequency of treatment:
Post. obs. period:
Doses:
Control Group: no data specified
Method:
Year: 1984 **GLP:** no data
Test substance: no data
Remark: "Chronic" exposure to 0.08 mg/m3 TA decreased the intensity of noradrenalime uptake.
At 0.4 mg/m3, the uptake was decreased by 25%.
At 1 mg/m3, the uptake decrease was 62%.

Exposure to 0.08 and 0.4 mg/m3 caused some increase in monoamine oxidose of the cerebral hemisphere, and at 1 mg/m3 increased enzyme was 26%.

Catechlomine o-methyltransferase activity also increased in the cerebrak hemisohere at 0.4 mg/m3, being higher at 1 mg/m3.

Reported to presumably affect the catecholarine inactivation mechanism of the CNS.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(141)

Species: rat **Sex:** no data
Strain:
Route of admin.: inhalation
Exposure period: 5 days
Frequency of treatment: daily
Post. obs. period:
Doses: 2 - 5 mg/m3
Control Group: no data specified
Method:
Year: 1965 **GLP:** no data
Test substance: no data
Remark: 5 daily 2-hr exposure

Mucous membrane redness
Increase in respiration rate recorded
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(142)

Species: rat **Sex:**
Strain:
Route of admin.: inhalation
Exposure period: 4 Wochen
Frequency of treatment: 6 h/Tag, 5 Tage/Woche
Post. obs. period:
Doses: 25 mg/m3
Control Group: no data specified
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Result: Keine Effekte von toxikologischer Relevanz.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(35)

Species: rat **Sex:** male
Strain: Sprague-Dawley
Route of admin.: inhalation
Exposure period: 6 Monate
Frequency of treatment: 6 h/Tag, 5 Tage/Woche
Post. obs. period:
Doses: 10 mg/m3
Control Group: no data specified
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Result: Keine Befunde von toxikologischer Relevanz.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(143)

Species: rat **Sex:** male/female
Strain:
Route of admin.: inhalation
Exposure period: 4 Wochen
Frequency of treatment: 6 h/Tag, 5 Tage/Woche
Post. obs. period:
Doses: 0, 0.52, 1.19, 3.31 mg/m3
Control Group: yes
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: 10 Tiere/Gruppe/Geschlecht
Result: Histopathologisch wurde bei 19/20 Tieren der 3.31 mg/m3-Gruppe (Kontrolle 1/20) Degeneration des Tracheaepithels festgestellt, jedoch zeigten die Lungenfunktionsprüfungen keine Unterschiede zwischen den Gruppen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(144)

Species: rat **Sex:** no data
Strain: no data
Route of admin.: oral feed
Exposure period: 90 days
Frequency of treatment:
Post. obs. period:
Doses: 1%
Control Group: no data specified
NOAEL: = 750 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: other TS
Source: INCA INTERNATIONAL S.p.A. Milan
Test substance: TPA, no indication about purity.

(145)

date: 22-FEB-2000
5. Toxicity Substance ID: 100-21-0

Species: rat **Sex:** male/female
Strain:
Route of admin.: oral feed
Exposure period: 90 days
Frequency of treatment: continuous
Post. obs. period:
Doses: 3% in the diet
Control Group: yes, concurrent no treatment
Method: other
Year: 1975 **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Remark: Parameters Monitored during the study - Body weight, Food consumption, Haematology, Blood Chemistry, Urinalysis, Gross Necroscopy, Mortality, Behaviour, Organ weights, Interim sacrifice
Result: Haematuria and crystalluria were prevalent after 60 days. There was a high incidence of urinary bladder calculi noted. Kidney calculi were less prevalent. It is believed that the bladder calculi were formed as a result of a supersaturated solution of phthalates in the excreted urine. This effect was only seen at high oral doses and animals ingesting less than 1% in the diet did not have significant calculi present. Histopathology revealed mild to moderate urinary bladder epithelial hyperplasia in the form of epithelial thickening. It is believed that this effect was secondary to the chronic physical injury by the bladder calculi. There was no evidence of neoplastic change and these effects were limited to high dose groups.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (146)

Species: rat **Sex:** male/female
Strain:
Route of admin.: oral feed
Exposure period: 105 days
Frequency of treatment: continuous
Post. obs. period: 0 days
Doses: 0.05, 0.16, 0.5, 1.6, 5.0% w/w
Control Group: yes, concurrent no treatment
Method: other
Year: 1970 **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Parameters Monitored during the study - Body weight, Food consumption, Haematology, Blood Chemistry, Urinalysis, Gross Necroscopy, Mortality, Behaviour, Organ weights, Interim sacrifice
Result: Slight retardation in growth occurred in the highest dose group even though food consumption appeared to be normal. Gross pathology revealed haematuria, urinary cystitis and urinary calculi formation. Calculi were limited to male rats of the highest dose group and were formed as a result of a supersaturated solution of phthalates in the urine. Histopathology revealed epithelial hyperplasia of the

urinary bladder in the high dose males. It is believed that this effect was secondary to the chronic irritation induced by the bladder calculi. The bladder calculi and subsequent inflammation and hyperplasia seem to be threshold effects in that only animals in the high dose group (5%) displayed this pattern of pathology.

Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (147)

Species: rat **Sex:** male/female
Strain:
Route of admin.: oral feed
Exposure period: 15 weeks
Frequency of treatment: daily
Post. obs. period:
Doses: 25, 80, 250, 800, 2500 mg/kg/day
Control Group:
Method:
Year: 1972 **GLP:** no data
Test substance: no data
Remark: 800 mg/kg - significant increase in amount on TA in blood. TA excreted in the urine in all dose groups.

2500 mg/kg - haematuria and bladder stones.

Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (148)

Species: rat **Sex:** male/female
Strain:
Route of admin.: oral feed
Exposure period: 90 days
Frequency of treatment: daily
Post. obs. period:
Doses: 1%, 3.2% or 10% (500, 1600, 500 mg/kg/day)
Control Group: yes, concurrent no treatment
NOAEL: 500 mg/kg bw
Method:
Year: 1972 **GLP:** no data
Test substance: no data
Remark: 10% considerable body weight reduction, haematuria, and effects on visual calculus. 4/12 animals died. Almost all animals had severe damage of ureter, as stones.

3.2%, 2/12 animals - ureter damage observed.

Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (148)

Species: rat **Sex:** male/female
Strain: Wistar
Route of admin.: oral feed
Exposure period: 13 weeks
Frequency of treatment: daily
Post. obs. period:
Doses: 5% for 1 week + 3% for 12 weeks
Control Group: no data specified
Method:
Year: 1972 **GLP:** no data
Test substance: no data
Remark: Bladder stones induced in 11/18 males and 3/19 females sacrificed after 90 days.

Strong correlation found between the presence of uroliths and the development of bladder hyperplasia : 62% of males (8/13) and 100% of females (3/3) diagnosed as having transitional cell hyperplasia also had bladder stones.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(149)

Species: rat **Sex:** no data
Strain:
Route of admin.: oral feed
Exposure period: 90 days
Frequency of treatment: daily
Post. obs. period:
Doses: 1, 3.2, 10% in diet
Control Group: no data specified
Method:
Year: 1981 **GLP:** no data
Test substance: no data
Remark: 1% : slight anaemia
3.2% : signs of urine retention
10% : reduced growth rate, anaemia, considerable urine retention
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(150)

Species: rat **Sex:** female
Strain: Wistar
Route of admin.: oral feed
Exposure period: 7 days
Frequency of treatment: daily
Post. obs. period:
Doses: 310 mg/kg/day
Control Group: yes, concurrent no treatment
Method:
Year: 1968 **GLP:** no data
Test substance: no data
Remark: No effects on content of sugar, protein or nitrogen in plasma.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (151)

Species: rat **Sex:** male/female
Strain:
Route of admin.: oral feed
Exposure period: 2 weeks
Frequency of treatment: daily
Post. obs. period:
Doses: 650-2000 mg/kg/day
Control Group: no data specified
NOAEL: 1500 mg/kg
Method:
Year: 1981 **GLP:** no data
Test substance: no data
Remark: 2000 mg/kg/day produced urinary tract calculi (stones) in young rats within 2 weeks.

Increases in urine calcium levels and a reduction in urinary pH occured in rats given diets of 650 mg/kg/day for 2 weeks.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (150)

Species: rat **Sex:** male/female
Strain: Wistar
Route of admin.: oral feed
Exposure period: 90 days
Frequency of treatment: daily
Post. obs. period:
Doses: 0.03 - 5.0% diet (ie. 15, 62.5, 250, 1000, 2500 mg/kg/day)
Control Group: yes, concurrent no treatment
Method:
Year: 1982 **GLP:** no data
Test substance: no data
Remark: 1000 mg/kg - effects on the urinary tract, especially the bladder. Dietary level 5% - deaths occured.

Indications of a reduced weight gain were seen throughout the testefd dose range of 0.03 - 5.0% diet.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(152)

Species: rat **Sex:** male/female
Strain: Wistar
Route of admin.: oral feed
Exposure period: 2 yr
Frequency of treatment: daily
Post. obs. period:
Doses: 142, 1000 mg/kg/day
Control Group: yes, concurrent no treatment
Method:
Year: 1983 **GLP:** no data
Test substance: no data
Remark: Effects on turinary tract, bladder most commonly involved - 1000 mg/kg/day.
Increases in liver weight - 1000 mg/kg/day.

No effects observed when administered 142 mg/kg/day.

Urinary tract calculi (Stones) in rats given 1000 mg/kg but not in those given 142 mg/kg.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(153)

Species: rat **Sex:** male
Strain:
Route of admin.: oral feed
Exposure period: 14 days
Frequency of treatment: daily
Post. obs. period:
Doses: 4%
Control Group: yes, concurrent no treatment
Method:
Year: 1983 **GLP:** no data
Test substance: no data
Remark: 50% incidence of bladder calculi, aciduria, elevated urinary excretion of cadmium and magnesium. Slightly elevated serum levels of Ca and Mg.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(154)

Species: rat **Sex:** female
Strain: other: Wistar King-A
Route of admin.: oral feed
Exposure period: 7 Tage
Frequency of treatment: taeglich
Post. obs. period:
Doses: 0, 310 mg/kg Kgw.
Control Group: no data specified
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Result: Keine Einfluss auf den Gehalt an Zucker, Protein und Stickstoff (Aminosaeuren, Harnstoff) im Plasma.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire

(116)

Species: rat **Sex:** female
Strain: other: Wistar King-A
Route of admin.: oral feed
Exposure period: 7 Tage
Frequency of treatment: täglich
Post. obs. period:
Doses: 0, 310 mg/kg Kgw.
Control Group: no data specified
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Result: Keine Einfluß auf den Gehalt an Zucker, Protein und Stickstoff (Aminosäuren, Harnstoff) im Plasma.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(116)

Species: rat **Sex:** male/female
Strain:
Route of admin.: oral feed
Exposure period: 2 Wochen (18. - 42. Tag postnatal)
Frequency of treatment: täglich
Post. obs. period:
Doses: 5 %
Control Group: no data specified
NOAEL: < 1.5 %
Method:
Year: **GLP:**
Test substance:
Result: M: 93.3 % Blasensteine; w: 73.3 % Blasensteine; Hyperplasie des Übergangsepithels in den Harnblasen, die Steine enthalten.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(155)

Species: rat **Sex:**
Strain:
Route of admin.: oral feed
Exposure period: 90 Tage
Frequency of treatment: täglich
Post. obs. period:
Doses: 1, 3.2, 10 %
Control Group: no data specified
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Result: 1 %: Geringgradige Anämie; 3.2 % veränderte Harnzusammensetzung; 10 % Wachstumsverzögerung, Anämie, erhebliche Harnkonkrementbildung
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(155)

date: 22-FEB-2000
5. Toxicity Substance ID: 100-21-0

Species: rat **Sex:** male
Strain: Fischer 344
Route of admin.: oral feed
Exposure period: 2 Wochen (28. - 42. Tag postnatal)
Frequency of treatment: täglich
Post. obs. period:
Doses: 0, 4 %
Control Group: yes
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Junge Tiere
Result: Reduktion des Körpergewichtes um 20 %, bei 50 % der Tiere Blasensteine, erhöhte Wasseraufnahme und ausgeprägte Hyperazidität des Urins sowie erhöhte Kalzium- und Magnesiumspiegel im Urin.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(156)

Species: rat **Sex:** male/female
Strain: Fischer 344
Route of admin.: oral feed
Exposure period: 2 Wochen (28. - 42. Tag postnatal)
Frequency of treatment: täglich
Post. obs. period:
Doses: 0, 0.5, 1.5, 3, 4, 5 % (500, 1500, 3000, 4000, 5000 mg/kg Kgw.)
Control Group: yes
NOAEL: 1.5 %
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Junge Tiere
Result: Bei den beiden höchsten Dosierungen reduzierte Körpergewichtsentwicklung (ab dem 34. Tag postnatal) sowie ab 3 % im Futter vermehrter Wasserverbrauch (ab 34. Tag postnatal) und Diarrhoe (vermutlich wegen unvollständiger Resorption der Substanz), ab 3 % im Futter (3700 mg/kg Kgw./Tag) dosisabhängig erhöhte Bildung von Blasensteinen (m: 3/30, 17/30, 28/30: w: 1/30, 6/30, 22/30), gleichzeitig Hyperplasie des Blasenwandepithels und Hämaturie, nur bei Tieren mit Blasensteinen histologische Veränderungen in der Blase.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(155)

date: 22-FEB-2000
5. Toxicity Substance ID: 100-21-0

Species: rat **Sex:** male/female
Strain: Wistar
Route of admin.: oral feed
Exposure period: 13 Wochen
Frequency of treatment: täglich
Post. obs. period:
Doses: 0, 5 % (1. Woche) bzw. 3 % (restliche 12 Wochen)
Control Group: yes
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Dosierung: 2500 mg/kg Kgw., erste Woche bzw. 1500 mg/kg Kgw. restliche 12 Wochen
Result: Bildung von Blasensteinen bei 11/18 m und 3/19 w, keine Anzeichen von neoplastischen Veränderungen, enge Korrelation zwischen dem Auftreten von Blasensteinen und der Entwicklung von Blasenhyperplasie (62 % der m und 100 % der w hatten gleichzeitig Blasensteine und eine Übergangsepithelhyperplasie der Blase).
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(143) (157)

Species: rat **Sex:** male/female
Strain: other: Wistar, Sprague-Dawley
Route of admin.: oral feed
Exposure period: 90 Tage
Frequency of treatment: täglich
Post. obs. period:
Doses: 0, 0.03, 0.125, 0.5, 2, 5 % (15, 62.5, 250, 1000, 2500 mg/kg Kgw.)
Control Group: yes
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Result: Die m Wistar-Ratten waren hinsichtlich der Bildung von Blasensteinen wesentlich empfindlicher als die m Sprague-Dawley-Ratten (Wistar m: 1/5 der 5 %-Gruppe nach 30 Tagen, 1/10 der 0.03 %-Gruppe nach 90 Tagen, 4/10 der 5 %-Gruppe nach 90 Tagen; Sprague-Dawley m: keine Blasensteine), bei 1/10 w Wistar-Ratten und 1/10 w Sprague-Dawley-Ratten ebenfalls Blasensteine in der 5 %-Gruppe, gleichzeitig leichte bis mittlere Hyperplasie des Übergangsepithels (Wistar: m 3/9, w 5/10; Sprague-Dawley: m 1/10, w 4/10).
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(158)

Species: rat **Sex:** male/female
Strain:
Route of admin.: oral feed
Exposure period: 90 Tage
Frequency of treatment: täglich
Post. obs. period:
Doses: 0, 1, 3.2, 10 % (500, 1600, 5000 mg/kg Kgw.)
Control Group: yes
NOAEL: 1 %
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: 6 Tiere/Gruppe/Geschlecht
Result: In der höchsten Dosisgruppe beträchtliche Körpergewichtsreduktion, Hämaturie und Blasensteine, 4/12 Tiere starben, bei allen Tieren schwere Schäden der Harnleiter aufgrund der Steine, in der mittleren Dosisgruppe bei 2/12 Tieren pathologische Befunde der Harnleiter aufgrund von Steinen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(157)

Species: rat **Sex:** male/female
Strain:
Route of admin.: oral feed
Exposure period: 15 Wochen
Frequency of treatment: täglich
Post. obs. period:
Doses: 0, 0.05, 0.16, 0.5, 1.6, 5 % (25, 80, 250, 800, 2500 mg/kg Kgw.)
Control Group: yes
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Result: Ab 1.6 % im Futter signifikant erhöhte Terephthalsäuremengen im Blut, quantitative Exkretion der Terephthalsäure über den Urin in allen Dosisgruppen, bei den m der 5 %-Gruppe Hämaturie und Blasensteine.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(157)

Species: rat **Sex:** female
Strain:
Route of admin.: i.p.
Exposure period: 102 days
Frequency of treatment: every 7 days
Post. obs. period:
Doses: 0.3 - 0.6 ml/animal (15% suspension olive oil)
Control Group: no data specified
Method:
Year: 1966 **GLP:** no data
Test substance: no data
Remark: After 6 weeks, reduced body weight. No adverse toxic effect or pathological findings observed.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(159)

Species: rat **Sex:** no data
Strain: Sprague-Dawley
Route of admin.:
Exposure period:
Frequency of treatment: no data
Post. obs. period:
Doses: 20 mg/kg/day
Control Group: no data specified
Method:
Year: 1993 **GLP:** no data
Test substance: no data
Remark: As cited in Toxline Datastar Subfile.

Lowered serum cholestrol and triglyceride levels.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(160)

Species: rat **Sex:** female
Strain:
Route of admin.: i.p.
Exposure period: 102 Tage
Frequency of treatment: jeden 7. Tag
Post. obs. period:
Doses: 0.3 - 0.6 ml/Tier einer 15 %igen Suspension in Olivenöl
Control Group: no data specified
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: 10 Tiere; Gesamtdosis: 1100 mg/Tier
Result: Ab der 6. Woche reduzierte Körpergewichtsentwicklung, ansonsten weder Intoxikationserscheinungen noch pathologische Befunde.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(102)

Species: mouse **Sex:** female
Strain: Swiss
Route of admin.: oral feed
Exposure period: 7 days
Frequency of treatment: daily
Post. obs. period:
Doses: 766 mg/kg/day
Control Group: yes, concurrent no treatment
Method:
Year: 1968 **GLP:** no data
Test substance: no data
Remark: Reduction in sleeping time, indication of induction of microsomal enyzmes.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (151)

Species: mouse **Sex:** female
Strain: Swiss
Route of admin.: oral feed
Exposure period: 7 days
Frequency of treatment: daily
Post. obs. period:
Doses: 852 mg/kg
Control Group: yes, concurrent no treatment
Method:
Year: 1968 **GLP:** no data
Test substance: no data
Remark: Significant decrease in bromosulphalein retention.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (151)

Species: mouse **Sex:** female
Strain: Swiss
Route of admin.: oral feed
Exposure period: 7 days
Frequency of treatment: daily
Post. obs. period:
Doses: 801 mg/kg
Control Group: yes, concurrent no treatment
Method:
Year: 1968 **GLP:** no data
Test substance: no data
Remark: No effect on the activities of GOT and GPT in plasma. No damage to liver cells.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (151)

Species: mouse **Sex:** female
Strain: Swiss
Route of admin.: oral feed
Exposure period: 7 days
Frequency of treatment: daily
Post. obs. period:
Doses: 815 mg/kg
Control Group: yes, concurrent no treatment
Method:
Year: 1968 **GLP:** no data
Test substance: no data
Remark: No effects on liver function.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(151)

Species: mouse **Sex:** no data
Strain:
Route of admin.: oral feed
Exposure period: 7 days
Frequency of treatment: daily
Post. obs. period:
Doses: 800 mg/kg/day
Control Group: no data specified
Method:
Year: 1968 **GLP:** no data
Test substance: no data
Remark: No evidence of affecting kidney function or inducing liver injury.
Some evidence that the liver enzyme activity may have been stimulated.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(151)

Species: mouse **Sex:** female
Strain: Swiss
Route of admin.: oral feed
Exposure period: 7 Tage
Frequency of treatment: täglich
Post. obs. period:
Doses: 0, 815 mg/kg Kgw.
Control Group: yes
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: 10 Tiere/Gruppe
Result: Keine Veränderung der Nierenfunktion.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(116)

Species: mouse **Sex:** female
Strain: Swiss
Route of admin.: oral feed
Exposure period: 7 Tage
Frequency of treatment: täglich
Post. obs. period:
Doses: 0, 801 mg/kg Kgw.
Control Group: yes
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: 15 Tiere/Gruppe
Result: Kein Einfluß auf die Aktivität von GOT und GPT im Plasma, keine Schädigung der Leberzellen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(116)

Species: mouse **Sex:** female
Strain: Swiss
Route of admin.: oral feed
Exposure period: 7 Tage
Frequency of treatment: täglich
Post. obs. period:
Doses: 0, 852 mg/kg Kgw.
Control Group: yes
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: 10 Tiere/Gruppe
Result: Signifikante Abnahme der Bromsulfophthalein-Retention.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(116)

Species: mouse **Sex:** female
Strain: Swiss
Route of admin.: oral feed
Exposure period: 7 Tage
Frequency of treatment: täglich
Post. obs. period:
Doses: 0 (35 Tiere), 766 mg/kg Kgw. (20 Tiere)
Control Group: yes
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Result: Verkürzung der durch Hexobarbital induzierten Schlafzeit (Hinweis auf die Induktion mikrosomaler Enzyme).
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(116)

Species: guinea pig **Sex:** male
Strain: Hartley
Route of admin.: inhalation
Exposure period: 6 months
Frequency of treatment: 6 hr/day, 5 days/week
Post. obs. period:
Doses: 10 mg/m3
Control Group: yes, concurrent no treatment
Method:
Year: 1982 **GLP:** no data
Test substance: no data
Remark: 10 mg/m3 - "respirable" dust concn = 5 mg/m3
No effects on body weights, organ (lung, liver, kidney, spleen) weights, clonical chemistry or tissue structure.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(138) (139)

Species: guinea pig **Sex:** male
Strain: Hartley
Route of admin.: inhalation
Exposure period: 6 Monate
Frequency of treatment: 6 h/Tag, 5 Tage/Woche
Post. obs. period:
Doses: 10 mg/m3
Control Group: no data specified
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Result: Keine Befunde von toxikologischer Relevanz.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(143)

Species: other **Sex:** no data
Strain:
Route of admin.: oral feed
Exposure period:
Frequency of treatment: no data
Post. obs. period:
Doses: 0.5% in diet
Control Group: no data specified
Method:
Year: 1965 **GLP:** no data
Test substance: no data
Remark: Species: chicken

Reduced body weight, inhibited sperm formation, induced testes damage, and effects on the pituitary and thyroid.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(161)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella TA100, TA1535, TA1537, TA1538, TA98
Concentration: 333.3 microgram/plate
Metabolic activation: with and without
Result: negative
Method: other
Year: 1979 **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Precipitation at 10 mg/plate prevented retesting at higher doses.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(162)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration:
Metabolic activation: with and without
Result: negative
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(163)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration:
Metabolic activation: with and without
Result: negative
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Metabolische Aktivierung: +/- (Ratte, Hamster)
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(164)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1538
Concentration:
Metabolic activation: with and without
Result: negative
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(165)

Type: Ames test
System of testing: Salmonella TA98, TA100, TA1535, TA1538
Concentration:
Metabolic activation: with and without
Result: negative
Method:
Year: 1989 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(166)

Type: Ames test
System of testing: Salmonella TA98, TA100, TA1535, TA1537
Concentration:
Metabolic activation: with and without
Result: negative
Method:
Year: 1985 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(167)

Type: Ames test
System of testing: Salmonella TA100, TA98, TA97, TA102
Concentration:
Metabolic activation: with and without
Result: negative
Method:
Year: 1989 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(168)

Type: Ames test
System of testing: Salmonella TA97, TA98, TA100, TA102
Concentration:
Metabolic activation: with and without
Result: negative
Method:
Year: 1989 **GLP:** no data
Test substance: other TS
Remark: Pyrotechnically disseminated TA
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(169)

Type: Ames test
System of testing: Salmonella TA98, TA100, TA1535, TA1537
Concentration: up to 10 mg/plate
Metabolic activation: with and without
Result: negative
Method:
Year: 1984 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(170)

Type: Ames test
System of testing: Salmonella TA98, TA100, TA1535, TA1537
Concentration:
Metabolic activation: with and without
Result: negative
Method:
Year: 1982 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(171)

date: 22-FEB-2000

5. Toxicity Substance ID: 100-21-0

Type: Ames test
System of testing: Salmonella TA98, TA100, TA1535, TA1537
Concentration:
Metabolic activation: with and without
Result: negative
Method:
Year: 1980 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (172)

Type: Bacterial gene mutation assay
System of testing: Salmonella typhimurium TA 1535, TA 1537, TA 98, TA 100.
Concentration: 10mg/plate
Metabolic activation: with and without
Result: negative
Method: other
Year: **GLP:** no data
Test substance: other TS
Remark: Test method: "The chemical was tested, under code, in a preincubation of plate incorporation assay (Ames et Al., 1975); details of protocol are described elsewhere (Hawhort et Al. 1983). Briefly, overnight cultures of Salmonella were used Without metabolic activation or with metabolic activation (S-9 fraction). Approximately 10(E8) bacteria were mixed with 0.5ml of either 0.1M sodium phosphate buffer (pH=7.4) or S-9 mix (containing 10% S-9 fraction), and 50 or 100µl of the test chemical or solvent, in each of three tubes. This mixture was incubated at 37°C for 20 min, following which 2ml of molten top agar containing a trace amount of biotin and a growth-limiting amount of histidine (0.05mM each) was added. The mixture was then poured onto minimal agar plates and incubated at 37°C for 48 hr, after which time histidine-revertant colonies were counted. The chemical was tested at five dose levels, separated by half-log intervals. The high dose was 10mg/plate unless limited by solubility (determined visually) and/or toxicity. The final dose level selection was based on the results of a preliminary range-finding study conducted with TA 100 in the presence and absence of S-9. All tests were repeated at least once. Positive control chemicals used were: TA 1535, and TA 100, sodium azide; TA 98, 4-nitro-o-phenylenediamine; and TA 1537, 9-aminoacridine. 2-Aminoanthracene was used as the positive control for metabolic activation in all strains. Concurrent solvent and positive controls were included in all experiments. A mutagenic response was defined as a reproducible, dose-related increase in the number of histidine-independent colonies over the spontaneous incidence; there was no requirement for a specific magnitude of increase. Decoding took place after all testing was completed and the data were evaluated for the chemical."

Test results: "TPA was not mutagenic for Salmonella either without metabolic activation or with S-9 fraction".
Source: INCA INTERNATIONAL S.p.A. Milan
Test substance: TPA 98%.

(173)

Type: Cytogenetic assay
System of testing: CHL
Concentration: 2000 µg/ml
Metabolic activation: without
Result: negative
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: 48 h
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(174)

Type: Cytogenetic assay
System of testing: Human peripheral blood lymphocytes
Concentration:
Metabolic activation: no data
Result: negative
Method:
Year: 1989 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(168)

Type:
System of testing: DNA amplification test
Concentration:
Metabolic activation: no data
Result: negative
Method:
Year: 1989 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(168)

Type:
System of testing: Chinese hamster lung fibroblasts
Concentration: 2000 mg/ml (12 mm)
Metabolic activation: without
Result: negative
Method:
Year: 1988 **GLP:** no data
Test substance: no data
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(175)

Type: other
System of testing: Human peripheral blood lymphocytes
Concentration:
Metabolic activation: no data
Result: negative
Method:
Year: 1989 **GLP:** no data
Test substance: no data
Remark: Cells examined for micronucleii.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(168)

Type: other
System of testing: Primary rat hepatocytes
Concentration:
Metabolic activation: no data
Result: negative
Method:
Year: 1989 **GLP:** no data
Test substance: no data
Remark: Analysis for DNA single strand breaks.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(168)

5.6 Genetic Toxicity 'in Vivo'

Type: Micronucleus assay
Species: mouse **Sex:**
Strain:
Route of admin.: i.p.
Exposure period: single (examined at 24, 48 and 72 hrs)
Doses: 0.09 - 4.30 mmol/kg
Result:
Method:
Year: 1989 **GLP:** no data
Test substance: no data
Remark: Positive : Increase in micronuclei in bone marrow polychromatic crythrocytes - peak @ 24 hrs.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (176)

Type:
Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Doses:
Result:
Method:
Year: **GLP:**
Test substance:
Remark: No evidence of mutagenicity was seen in the bacterium Salmonella typhimurium, either in the presence or absence of a liver metabolising fraction (Ames test) (Florin et al. 1980; Sarrif, 1984; Zeiger et al. 1983).
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Type:
Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Doses:
Result:
Method:
Year: **GLP:**
Test substance:
Source: INCA INTERNATIONAL S.p.A. Milan

5.7 Carcinogenicity

Species: rat **Sex:** male/female
Strain: Wistar
Route of admin.: oral feed
Exposure period: 2 years
Frequency of treatment:
Post. obs. period:
Doses: 1, 2, 5% TPA
Result:
Control Group: no data specified
Method: other
Year: **GLP:** no data
Test substance: other TS
Remark: Test method: "Group of wistar Rats were fed diets containing 1, 2, or 5% TPA for two years".

Test results: "The significant findings of this study are:

1) TPA feeding inhibits growth at the 2% and 5% level in males and at 5% level in females.

2) TPA causes a decrease in the relative weights of some organs. At 1% level, liver weight is decreased in females, and the kidney is relatively smaller in both sexes. At 2% level, the relative weight of the liver, and heart are decreased only in females. At the 5% level, there is a significant increase in kidney weight in the males and an increased adrenal weight in both sexes.

3) There was an increased mortality in the 5% TPA groups which started approximately the second month of feeding. 1% and 2% TPA feeding had no effect on survival.

4) The predominant cause of morbility and mortality in the 5% group was due to the formation of TPA stones in the urinary tract. There was resultant Hydronephrosis and Pyelonephritis. The presence of stones caused changes in the epitelium of the urinary tract ranging through Hyperplasia, Papilloma, Squamous Metaplasia to both transitional cell tumors or sqamous cell carcinomata. The incidence of Nephropathy was also reflected by an increase in blood urea content.

5) TPA feeding did not cause an increase of spontaneous tumor. In the 5% groups there was a significant decrease in mammary tumor incidence in the females and thyroid medullary carcinoma in the males.

6) TPA feeding at <1% of the diet had no demonstrable toxicity for Rats of the wistar strain".
Source: INCA INTERNATIONAL S.p.A. Milan
Test substance: TPA, no indication about purity.

(177)

date: 22-FEB-2000

5. Toxicity Substance ID: 100-21-0

Species: rat **Sex:** male/female
Strain:
Route of admin.: oral feed
Exposure period: lifetime (2 years)
Frequency of treatment: continuous
Post. obs. period:
Doses: 0, 20, 142, 1000 mg/kg/day
Result:
Control Group: yes, concurrent no treatment
Method: other
Year: 1983 **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Remark: 126 animal per dose group (test and control)
Parameters Monitored during the study - Body weight, Food consumption, Haematology, Blood Chemistry, Urinalysis, Gross Necroscopy, Histopathology, Tumour development, Mortality, Organ weights, Interim sacrifice
Result: Terephthalic acid induced bladder stones were seen in 13/126 females in the high dose group. At the scheduled 6 and 12 month sacrifices, no bladder calculi were detected. At the 18 month sacrifice sand like particle or bladder calculi were only seen in two of the high dose females. There were 19/118 females with what was described as transitional cell adenomas by one pathology laboratory and epithelial hyperplasia by another. Two of these were detected in high dose females after 18 months (2/27), 15 were seen in seen in high dose females a t the end of the study (15/79), and one was seen in a control female at the end of the study. None were found in the males, nor at any other dose level. It was believed that rats fed high concentrations of terephthalic acid in the diet develop bladder calculi which appear to cause chronic inflammation of the bladder epithelium, bladder hyperplasia and subsequently bladder tumours. AN apparent threshold effect exists because animals exposed to lower concentrations for their lifetime do not form bladder calculi or tumours. The high dose group in this study (1000 mg/kg/day) corresponds to an approximate dietary concentration of 2.0% to 2.8% in adult Fisher rats.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(178)

Species: rat **Sex:** no data
Strain:
Route of admin.: oral feed
Exposure period: 2 years
Frequency of treatment: daily
Post. obs. period:
Doses: up to 5% diet max
Result:
Control Group: no data specified
Method:
Year: 1975 **GLP:** no data
Test substance: no data
Remark: No evidence of any carcinogenic effects.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (179)

Species: rat **Sex:** male/female
Strain: Fischer 344/DuCrj
Route of admin.: oral feed
Exposure period: 2 years
Frequency of treatment: daily
Post. obs. period:
Doses: 20, 142 or 1000 mg/kg/day
Result:
Control Group: yes, concurrent no treatment
Method:
Year: 1983 **GLP:** no data
Test substance: no data
Remark: Other than bladder tumours, no significant increase in other tumour types reported in males and females fed 20, 142 or 1000 mg/kg/day in diet.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (180)

Species: rat **Sex:** male/female
Strain: Wistar
Route of admin.: oral feed
Exposure period: 2 years
Frequency of treatment: daily
Post. obs. period:
Doses: 1% (500 mg/kg/day) & 2% (1000 mg), 5% (2500 mg)
Result:
Control Group: no data specified
Method:
Year: 1974 **GLP:** no data
Test substance: no data
Remark: Malignant and benign tumours of the urinary tract (in the bladder or the ureter) developed in a high % of rats fed 5%. Similar tumours in rats fed 2%. Bladder tumour developed in 1/43 males and females fed 1% in diet.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(181)

Species: rat **Sex:** male/female
Strain: other: Wag/Rij-Wistar
Route of admin.: oral feed
Exposure period: 2 Jahre
Frequency of treatment: täglich
Post. obs. period:
Doses: 0, 1, 2, 5 % (500, 1000, 2500 mg/kg Kgw.)
Result:
Control Group: yes
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Result: Reduzierte Körpergewichtsentwicklung bei den m der 2- und 5 %-Gruppe und bei den w der 5 %-Gruppe, in der 1 %-Gruppe erniedrigte relative Lebergewichte bei den w sowie bei beiden Geschlechtern relativ kleinere Nieren, in der 2 %-Gruppe nur bei den w erniedrigte relative Leber-, Nieren- und Herzgewichte, in der 5 %-Gruppe bei den m Zunahme der Nierengewichte sowie bei beiden Geschlechtern Zunahme der Nebennierengewichte, in der höchsten Dosisgruppe erhöhte Mortalität vornehmlich aufgrund der erhöhten Inzidenz an Blasensteinen (5 %: m 42/47, w 39/42; 1 %: 1/48), außerdem erhöhte Inzidenz an Blasen- und Harnleiterneoplasien (5 %:m 21/37, w 21/34; 2 %: m 1/48, w 2/47; 1 %: m 1/43), keine erhöhte Spontantumorrate; nach Meinung des Autors führt die Gegenwart der Steine zu Veränderungen des Harntraktepithels mit der Inzidenz von Hyperplasie, Papillomen, schuppigen Metaplasien bis hin zu Übergangszelltumoren bzw. schuppigen Zellkarzinomen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(182)

Species: rat **Sex:** male/female
Strain: Fischer 344
Route of admin.: oral feed
Exposure period: 2 Jahre
Frequency of treatment: täglich
Post. obs. period:
Doses: 0, 20, 142, 1000 mg/kg Kgw.
Result:
Control Group: yes
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Result: Nur in der höchsten Dosisgruppe bei w (11/86) wurden Blasensteine gefunden; die relativ niedrige Inzidenz von Blasensteinen wird auf die vergleichsweise niedrige Dosis zurückgeführt; die histologische Untersuchung wurde von 2 verschiedenen Teams durchgeführt: Übergangszelladenome (w, hohe Dosis 15/79 bzw. 10/73, Kontrolle 1/83), Übergangszellkarzi-

nome (w, hohe Dosis 2/79 bzw. 1/73), Hyperplasie der Blasenschleimhaut (w, hohe Dosis 14/79 bzw. 23/73, mittlere Dosis 2/70, niedrige Dosis 7/76, Kontrolle 8/83; m, hohe Dosis 2/82 bzw. 0/80, mittlere Dosis 3/82, niedrige Dosis 9/82, Kontrolle 2/87).

Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(183)

Species: rat **Sex:**
Strain:
Route of admin.: oral feed
Exposure period: 2 Jahre
Frequency of treatment: täglich
Post. obs. period:
Doses: bis max. 5 %
Result:
Control Group: no data specified
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Result: Keine Hinweise auf eine kanzerogene Wirkung.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(184)

Species: mouse **Sex:** female
Strain: C3H
Route of admin.: oral feed
Exposure period: 12 months
Frequency of treatment: daily
Post. obs. period:
Doses: 2500 mg/kg/day (5%)
Result:
Control Group: no data specified
Method:
Year: 1973 **GLP:** no data
Test substance: no data
Remark: Significantly reduced number of mammary tumours. At 12 months, mammary tumours occurred in 78% of controls and in 50% of treated mice.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(185)

Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Post. obs. period:
Doses:
Result:
Control Group:
Method:
Year: **GLP:**
Test substance:
Remark: Non human.-
Oral. malignant and bening tumours of teh urinary tract (in the bladder or the ureter,the duct carrying urine from the kidney to the bladder) developed in a high proportion of rats maintained for 2 yr on a diet contained 5% terephthalic acid [about 2500 mg/kg bw/day)] (Gross, 1974). These same tumour types were also seen in rats receiving 1000 mg/kg bw/day for the same period (CIIT, 1983; Gross, 1974). In one experiment, a single male rat on a 1% diet [500 mg/kg bw/day] out of 43 male and ^presumably] an approximately equal number of females testad developed a bladder tumour types were seen in increased numbers when groups of around 80 male and 80 female rats received 20, 142 or 1000 mg/kg bw/day for 2 yr (CIIT, 1983).
A significately reduced number of mammary tumours developed in female mice maintained on diet containing 5% terephthalic acid [7500 mg/kg bw/day].
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Post. obs. period:
Doses:
Result:
Control Group:
Method:
Year: **GLP:**
Test substance:
Remark: The conducted tests were negative
Source: SIPET SpA Patrica (FR)

5.8 Toxicity to Reproduction

Type: Fertility
Species: rat **Sex:** male/female
Strain: Wistar
Route of admin.: oral feed
Exposure Period: days 6-15 gestation
Frequency of treatment: daily
Premating Exposure Period
male: 90 days
female: 90 days
Duration of test:
Doses: 0, 0.03, 0.125, 0.5, 2.0, 5.0% diet
Control Group: yes, concurrent no treatment
Method:
Year: 1982 **GLP:** no data
Test substance: no data
Remark: No effects on fertility, litter size and foetal malformation rates.

Survival of pups reduced in groups receiving 2% (1000 mg/kg/day) or 5% (2500 mg/kg/day).

Indications of reductions in maternal weight gains seen throughout the dose range, being more marked at 2% and 5%.

Increased number of adult deaths occured in the 5% group.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(186) (187)

Type: Fertility
Species: rat **Sex:** male/female
Strain: Fischer 344
Route of admin.: oral feed
Exposure Period: 6 Monate
Frequency of treatment: taeglich
Duration of test:
Doses: 0, 0.5, 2, 5 % (250, 1000, 2500 mg/kg Kgw.)
Control Group: yes
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Result: In allen Dosisgruppen signifikant gesteigerte Ca2+-, H+- und NH4+-Exkretion sowie sichtlich gesteigerte Phosphat-Exkretion im Urin, in der 5 %-Gruppe hatten 2/6 w nach 6 Monaten Blasensteine, in utero und postnatal exponierte Jungtiere der 5 %-Gruppe zeigten stark reduzierte Koerpergewichtsentwicklung und betraechtlich erhoehte neonatale Mortalitaet, am 35. Tag hatten 92 % der ueberlebenden Jungen dieser Gruppe Blasensteine.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(188)

date: 22-FEB-2000
5. Toxicity Substance ID: 100-21-0

Type: Fertility
Species: rat **Sex:** male/female
Strain: other: Wistar bzw. CD
Route of admin.: oral feed
Exposure Period: 90 Tage
Frequency of treatment: taeglich
Duration of test:
Doses: 0, 0.03, 0.125, 0.5, 2. 5 % (15, 62.5, 250, 1000, 2500 mg/kg Kgw)
Control Group: yes
Method: other: keine Daten
Year: **GLP:** no data
Test substance: no data
Remark: Nach 90 Tagen Bildung von 10 Paaren/Dosisgruppe und Verabreichung der entsprechenden Dosis im Futter waehrend der Verpaarungs-, Schwangerschafts-, Laktations- und Aufzuchtperiode.
Result: Kein Einfluss auf Fertilitaetsindex und Wurfgroesse, ab 2 % im Futter deutliche Effekte auf die Foeten und Neugeborenen (76 % der Wistar-Ratten bzw. 96 % der CD-Ratten wurden tot geboren; postnatale Letalitaet bei Wistar- und CD-Ratten betrug 50 %; reduzierte Koerpergewichte bei den Neugeborenen), bei 5 % im Futter am Tag 21 reduzierte Koerpergewichte der Wistar- und CD-Nachkommen.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire

(189)

Type: Fertility
Species: rat **Sex:** male/female
Strain: Fischer 344
Route of admin.: oral feed
Exposure Period: 6 Monate
Frequency of treatment: täglich
Duration of test:
Doses: 0, 0.5, 2, 5 % (250, 1000, 2500 mg/kg Kgw.)
Control Group: yes
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Result: In allen Dosisgruppen signifikant gesteigerte Ca2+-, H+- und NH4+-Exkretion sowie sichtlich gesteigerte Phosphat-Exkretion im Urin, in der 5 %-Gruppe hatten 2/6 w nach 6 Monaten Blasensteine, in utero und postnatal exponierte Jungtiere der 5 %-Gruppe zeigten stark reduzierte Körpergewichtsentwicklung und beträchtlich erhöhte neonatale Mortalität, am 35. Tag hatten 92 % der überlebenden Jungen dieser Gruppe Blasensteine.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(188)

date: 22-FEB-2000

5. Toxicity Substance ID: 100-21-0

Type: Fertility
Species: rat **Sex:** male/female
Strain: other: Wistar bzw. CD
Route of admin.: oral feed
Exposure Period: 90 Tage
Frequency of treatment: täglich
Duration of test:
Doses: 0, 0.03, 0.125, 0.5, 2. 5 % (15, 62.5, 250, 1000, 2500 mg/kg Kgw)
Control Group: yes
Method: other: keine Angaben
Year: **GLP:** no data
Test substance: no data
Remark: Nach 90 Tagen Bildung von 10 Paaren/Dosisgruppe und Verabreichung der entsprechenden Dosis im Futter während der Verpaarungs-, Schwangerschafts-, Laktations- und Aufzuchtperiode.
Result: Kein Einfluß auf Fertilitätsindex und Wurfgröße, ab 2 % im Futter deutliche Effekte auf die Föten und Neugeborenen (76 % der Wistar-Ratten bzw. 96 % der CD-Ratten wurden tot geboren; postnatale Letalität bei Wistar- und CD-Ratten betrug 50 %; reduzierte Körpergewichte bei den Neugeborenen), bei 5 % im Futter am Tag 21 reduzierte Körpergewichte der Wistar- und CD-Nachkommen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(189)

Type: Two generation study
Species: rat **Sex:** male/female
Strain: Wistar
Route of admin.: oral feed
Exposure Period: 90 days
Frequency of treatment:
Duration of test: 90 days
Doses: 0.5, 2 and 5% TPA
Control Group: no data specified
NOAEL Parental: = 2500 mg/kg bw
NOAEL F1 Offspr.: = 1500 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: other TS
Remark: Test method: "Rats were fed TPA for 90 days to females and males at doses of 0.5, 2, or 5%".

Test results: "Evaluations of the effects of TPA feeding on reproduction and fertility parameters showed no TPA-related changes. However, TPA at dietary concentrations of 2 or 5% caused dose-dependent lethal effects on newborn and young rats".
Source: INCA INTERNATIONAL S.p.A. Milan
Test substance: TPA, no indication about purity.

(190)

date: 22-FEB-2000

5. Toxicity Substance ID: 100-21-0

Type: other
Species: mouse **Sex:** male/female
Strain: C3H
Route of admin.: oral feed
Exposure Period:
Frequency of treatment:
Duration of test:
Doses:
Control Group: no data specified
Method:
Year: 1973 **GLP:** no data
Test substance: no data
Remark: Reproduction indices (interval between mating and birth of the pups, litter size, pup weights, growth rate) were normal in group of 31 females that were maintained throughout life on diet containing 0.5% (750 mg/kg/day) TA, and allowed to produce six litters.

Females were mated first after ^ 50 days treatment.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(185)

Type:
Species: **Sex:**
Strain:
Route of admin.:
Exposure Period:
Frequency of treatment:
Duration of test:
Doses:
Control Group:
Method:
Year: **GLP:**
Test substance:
Remark: No effects observed
Source: SIPET SpA Patrica (FR)

5.9 Developmental Toxicity/Teratogenicity

Species: rat **Sex:** female
Strain:
Route of admin.: inhalation
Exposure period: Days 6 to 15 of gestation
Frequency of treatment: 6 hours per day, 7 days per week
Duration of test: 10 days
Doses: 0, 1.0, 5.0, 10.0 mg/m3
Control Group: yes
NOAEL Teratogen.: > 10
Method: other
Year: 1989 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Parameters Monitored during the study - Body weight, Gross Necroscopy, Reproduction, Mortality, Organ weights.
Result: Units for NOEL are mg/m3.

There were no deaths during the study. There was a slight increase in the incidence of foetuses with rib anomalies in the 5.0 mg/m3 group, but statistical significance was achieved only when all the rib anomalies were considered together. They were not considered as an indicator of teratogenesis as they were common variations that did not follow a dose response relationship and were within the range of historical controls. No other signs of toxicity were present.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (191)

Species: rat **Sex:** female
Strain: Sprague-Dawley
Route of admin.: inhalation
Exposure period: days 6-15 gestation
Frequency of treatment: daily
Duration of test:
Doses: 0, 1, 5, 10 mg/m3
Control Group: yes, concurrent no treatment
Method:
Year: 1990 **GLP:** no data
Test substance: no data
Remark: No deaths and no signs of maternal toxicity.
No significant differences in mean dam body or uterus weights, liver weights, body weight gain, or pup viability.
No significant increase in the incidence of foetal malformations or abnormalities in exposed litters. A statistically significant increase in the incidence of foetuses with rib anomalies were observed in the 5 mg/m3 group - not considered to be a teratogenc event.

Conclusion:
Exposure to 1, 5, or 10 mg/m3 did not result in significant toxic or teratogenic effects in the dam or foetuses.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire (192)

Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Duration of test:
Doses:
Control Group:
Method:
Year: **GLP:**
Test substance:
Remark: Non ha causato malformazioni alla nascita negli animali. Sono stati osservati altri effetti sul feto solo a dosi che hanno causato effetti tossici sulla madre.

In studi a lungo termine sono sati evidenziati tumori maligni negli animali
Source: SIPET SpA Patrica (FR)

5.10 Other Relevant Information

Type: adsorption
Remark: Hoshi and Kuretani (1967) characterized the gastrointestinal absorption of [C-carboxyl]-terephthalic aid in female Wistar rats given a single gavage dose of 85 mg/kg. The compound was administered to groups of five rats as a suspension in a 0.5% sodium carboxymethylcellulose. The esophagus, stomach, small intestine, caecum and large intestine of rats were assayed for radioactivity 2, 4, 6, 8, 24 and 48 hours after administration. Urine and feces were collected from treated rats after 8, 24 and 48 hours, and assayed for radioactivity. Expired air and feces collected for 24 hours accounted for <0.04 and 3.3% of the total radioactivity administrated, respectively. The dose was absorbed rapidly, as it was excreted in the urine almost quantitatively by 48 hours. After examining the various gastrointestinal segments, the authors calculated that 70 and 26% of the administered dose was absorbed from the upper (ie. stomach and small intestine) and lower (ie, caecum and large intestine) portions, respectively.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(193)

Type: Chemobiokinetics general studies
Remark: Ratte (Sprague-Dawley), Maus (CF1), männlich (je 6 Tiere pro Gruppe), 20 mg/kg Kgw./Tag, p.o. über 14 Tage (Ratte) bzw. 10, 20, 40, 60 mg/kg Kgw./Tag, i.p. über 16 Tage (Maus)
Wirkung:
Signifikante Abnahme von Cholesterin und Triglyzeriden im Serum, da Terephthalsäure die regulatorischen Enzyme der Cholesterin-, Fettsäure- und Triglyzeridsynthese hemmt, außerdem die Cholesterinresorption aus dem Verdauungstrakt verhindert und die Lipidausscheidung in die Faeces fördert.
Source: Hoechst AG Frankfurt/Main

Hoechst Trevira GmbH & Co KG Frankfurt am Main
(194)

Type: Distribution
Remark: Hoshi and Kuretani (1968) studied the distribution of [C-carboxyl]-terephthalic acid in the female Wistar rat. Groups of five animals were given a single gavage dose of 85 mg terephthalic acid suspended in 0.5% sodium carboxymethylcellulose. Animals were killed and their blood and tissues assayed for radioactivity 2, 4, 6, 8, 24 and 48 hours after administration. Samples of plasma, kidney, liver, brain, skin, lung, pancreas, spleen, fat, heart, muscle, bone, erythrocytes, uterus, ovary and endocrine glands contained terephthalic acid up to 6 hours after administration, with the kidney having the highest concentrations, followed by the liver and plasma. No radioactivity was observed in any of the above tissues 48 hours after administration. The biological half-life of terephthalic acid in these tissues was 1.2-3.3 hours, and elimination followed first-order kinetics. Similar results were observed in rats and fed a diet containing 0.5% [C-carboxyl]-terephthalic acid for 1 or 3 days, and killed immediately or 1 day after exposure. These results showed that terephthalic acid was widely distributed in various body tissues, but did not accumulate in any of them.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(195)

Type: Distribution
Remark: Radioactivity labeled terephthalic acid was used to determine its mode of absorption, distribution, and excretion (Moffitt et al. 1975). Adult male rats were administered single (0-80 mg/kg 14C-TA) or multiple (5 doses totaling 0-80 mg/kg 14C-TA over 10 days) oral doses. It was found that more than 80% of a single dose of 14C-TA was excreted in the urine and feces within 48 hrs. of administration. After repeated dosing, more than 89% of the total administered was recovered in the urine and feces within 24 hours of the last dose. Negligible tissue absorption and accumulation in organs were recorded. Forty-eight hours after a single intratracheal dose (0-10 mg/kg), rats excreted 49-73% of the total administered; 45-66.6% was recovered in the urine and 3.4-6.4% in the feces. After repeated intratracheal exposures (5 doses totalling 0-10 mg/kg), less than one percent of the total dose was found in the lungs and tracheal lymph nodes, 24 hours after the last treatment. Insignificant amounts of terephthalic acid were detected in the other organs assayed.

Dermal and ocular application of terephthalic acid (TA) revealed negligble excretion and absorption following single, multiple, or long term exposure.
The direct instillation of up to 10 mg radiolabelled terephthalic acid (as a 1% solution in emulsified distilled water) into the lungs of rats, five times in 10 days produced no evidence of accumulation. Less than 1% of the administered dose was present in the lungs and windpipe

lymph nodes 24 hr after the final instillation. Negligible radioactivity (< 0.1% of dose) was detected in the other organs assayed.

Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(196)

Type: Excretion
Remark: "Between 20 and 40% of the TPA fed to Rats is absorbed and excreted by the Kidney. Only 6% of the acid not excreted in the urine appeared in the feces. The remainder is probably destroyed in the gut rather than absorbed and either matabolized or stored in the tissues".
Source: INCA INTERNATIONAL S.p.A. Milan
Test substance: TPA, no indication about purity.

(197)

Type: Excretion
Remark: Hoshi and Kuretani (1967) monitored the expired air, urine and feces of rats given a single gavage dose of 85 mg [C-carboxyl]-terephthalic acid suspended in 0.5% aqueous carboxymethylcellulose. Twenty-four hours after administration, the urine, feces and expired air accounted for 93.5, 3.3 and <0.04% of the radioactivity administered, respectively. After 48 hours, the integrated excretion of radioactivity in the urine and feces was 93.8 and 3.3% respectively.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(198)

Type: Excretion
Remark: Hoshi and Kuretani (1965) studied the excretion of terephthalic acid when given to rats by gavage, i.p. injection and dietary inclusion. when a gavage dose of 200 mg/kg suspended in 0.5% aqueous sodium carboxymethylcellulose was given to rats, terephthalic acid was found 24 hours after administration in the urine and feces, and accounted for -55 and 30% of the dose, respectively. When a similar dose was given by i.p. injection, most of the dose was recovered quantitatively in the urine after 24 hours. When fed 300 mg terephthalic acid/kg/day, rats excreted 78-85% of the dose in urine and the rest in feces by 24 hours after feeding. No other experimental details were found in the available abstract (Hoshi and Kuretani, 1965).
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(199)

Type: Excretion
Remark: The Renal Handling of Terephthalic Acid. TREMAINE L M AND QUEBBEMANN A J. (1985) Toxicol Appl Pharmacol 77, 165-174. By use of the Sperber in vivo chicken preparation method (1948 Ann R Agric Coll Swed 15, 317-349), infusion of radiolabeled terephthalic acid ([C]TPA) into the renal portal circulation revealed a first-pass excretion of the unchanged compound into the urine. This model was utilized further to characterize the excretory transport of [C]TPA and provide information on the structural specificity in the

secretion of dicarboxylic acids. At an infusion rate of 0.4 nmol/min 60% of the [C]TPA which reached the kidney was directly excreted. An infusion rate of 3 or 6 nmol/min resulted in complete removal of [C]TPA by the kidney. These results indicate that TPA is both actively secreted reabsorbed when infused at 0.4 nmol/min and that active reabsorption is saturated with the infusion of TPA at higher concentrations. The secretory process was saturated with the infusion of TPA at 40 nmol/min. The excretory transport of TPA was inhibited by the infusion of probenecid, salicylate, and m-hydroxybenzoic acid, indicating that these organic acids share the same organic anion excretory transport process m-Hydroxybenzoic acid did not alter the simultaneously measured excretory transport of p-aminohippuric acid (PAH), suggesting that there are different systems involved in the secretion of TPA and PAH. The structural specificity for renal secretion of dicarboxylic acids was revealed by the use of o-phthalic acid and m-phthalic acid as possible inhibitors of TPA secretion m-Phthalate, but not o-phthalate, inhibited TPA excretory transport, indicating that there is some specificity in the renal secretion of carboxy-substituted benzoic acids. TPA was actively accumulated by rat and human cadaver renal cortical slices.

Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(200)

Type: Excretion
Remark: Ratte (Charles River), männlich, 40, 80 mg/Tier, einmal bzw. 5mal in 10 Tagen, p.o.
Wirkung:
Innerhalb von 48 h Ausscheidung von >80 %, davon ca. 40 % im Urin und ca. 47 % im Kot; nach wiederholter Gabe Ausscheidung von >90 % in Urin und Kot, dagegen Nachweis von <0.1 % in Leber, Lunge, Herz, Nieren, Milz, Nebennieren, Pankreas, Hoden, Hirn und Femur.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(201)

Type: Excretion
Remark: Ratte (Charles River), männlich, 5, 10 mg/Tier, einmal bzw. 5mal in 10 Tagen, intratracheal
Wirkung:
Nach 48 h 45.7 - 66.6 % im Urin, 3.4 - 6.4 % im Kot (sowohl nach einmaliger als auch nach wiederholter Gabe), <1 % in Lunge und trachealen Lymphknoten, <0.1 % in Leber, Herz, Nieren, Milz, Nebennieren, Pankreas, Hoden, Hirn und Femur.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(201)

Type: Excretion
Remark: Ratte (Charles River), männlich, 80 mg in 0.2 ml wässriger Triton-X-Lösung/Tier, einmal bzw. 5mal in 10 Tagen, dermal (Rücken, okklusiv)
Wirkung:
Nach einmaliger Gabe über 24 h 1.6 % im Urin, 0.6 % im Kot, 1.9 % auf der behandelten Hautstelle, 0.7 % in der Leber und 0.3 % in Lunge, Herz, Nieren, Milz, Nebennieren, Pankreas, Hoden, Hirn und Femur; nach wiederholter Gabe über 10 Tage (24 h nach der letzten Applikation) 4.3 % im Urin, 2.2 % im Kot und 2.1 % in den übrigen Organen; keine Hautreizwirkung.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(201)

Type: Excretion
Remark: Kaninchen (Neuseeland), 50 mg/Tier, 5 min bzw. 24 h, ins Auge (Konjunktivalsack)
Wirkung:
Nach 5 min Exposition innerhalb von 10 Tagen 1.8 % im Urin, 0.5 % im Kot sowie <0.1 % im Auge und allen anderen Organen; nach 24 h Exposition innerhalb von 10 Tagen 6.1 % im Urin, 2.2 % im Kot und <0.1 % im Auge und den übrigen Organen.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(201)

Type: Excretion
Remark: Ratte (Wistar-King-A), 85 mg/kg Kgw., p.o.
Wirkung:
Nach 48 h 93.8 % im Urin und 3.3 % im Kot nachweisbar (folglich wurde die Substanz nicht metabolisiert).
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(202)

Type: Excretion
Remark: Ratte (F-344), männlich, i.v. bzw. p.o.
Wirkung:
Nach i.v.-Injektion wurde eine Plasma-Halbwertszeit von ca. 1.2 h gemessen, nach oraler Gabe 2.43 h; nach i.v.-Gabe wurde die Substanz nahezu 100 % innerhalb von 8 h über den Urin ausgeschieden, wonach es zu keiner Metabolisierung der Substanz kam; keine Angaben zur Eliminationsrate nach oraler Gabe.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(203)

Type: Excretion
Remark: Legehennen (Ross Arbor Acres), kontinuierliche Infusion über die renale Portalzirkulation
Wirkung:
Ca. 50 min nach Beginn der Infusion entnommene Urinproben zeigten, daß mehr als 85 % der Substanz im Urin vorhanden waren; der Hauptteil (60 %) wurde im "first pass" direkt über die Niere ausgeschieden.

Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main
(204)

Type: Metabolism
Remark: Chemical Urolithiasis 2. Thermodynamic Aspects of Bladder Stone Industion by Terephthalic Acid and Dimethyl Terephthalate in Weanling Fischer-344 Rats, Heck, H.d'A (1981). Fundam Appl Toxicol 1:299-308. The induction of calcium terephthalate (CaTPA) calculi in the urinary tract of rats ingesting terephthalic acid (TPA) or dimethyl terephthalate is a result of supersaturation with respect to the stone components. The solubility product of CaTPA was determined in water at 37 Deg C, and it value in urine of exposed weanling Fischer-344 rats was calculated based on the electrolyte concentrations of freshly-collected, microliter urine samples. The value of the solubility product in urine is equal to the minimum concentration product of free Ca and TPA at which crystallization can occur; hence, the urinary solubility product is a parameter that is useful for risk assessment. Estimates of the TPA concentrations required to induce crystals or stones in normal human urine are presented.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(205)

Type: Toxicokinetics
Remark: IV and oral administration.

The pharmacokinetics of (14C)terephthalic acid ((14C) TPA)were determined in Fischer-344 rats after intravenous and oral administration. After iv injection, the plasma concentration-time data were fitted using a three-compartment pharmacokinetic model. The average terminal half-life in three rats was 1.2 +/- 0.4 hr, and the average volume of distribution in the terminal phase was 1.3 +/- 0.3 liters/kg. Following administration by gavage, a longer terminal half-life was obtained, indicating that dissolution of (14C)TPA or absorption from the gut may be partially rate-limiting. Recovery of (14C)TPA in the urine following a bolus iv dose was 101 +/- 8%, indicating essentially complete urinary excretion of the compound. No evidence of metabolism of (14C)TPA was obtained by analysis of urine by high-performance liquid chromatography. (14C)TPA was transported to the fetus after administration of the compound to pregnant rats; however, the concentrations in fetal tissues were low relative to the corresponding maternal tissues. Neonatal rats exposed to 5% TPA in the diet of their dams did not develop calculi until the onset of self-feeding. These results demonstrate that TPA is rapidly excreted into urine after administration to rats, and that excretory mechanisms in the dam provide an effective mechanism of defense against TPA-induced urolithiasis in neonatal rats.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire
(206)

Type: other
Remark: Metabolism of terephthalic acid II. Plasma concentration of terephthalic acid and its biological half-life. Akio Hoshi, Junko Takagi, Reiko Yanai, and Kazuo Kuretani (Natl. Cancer Center, Tokyo). Yakugaku Zasshi 86(10), 963-7 (1966) (Japan); ef. CA 64, 2601b. Changes of terephthalic acid (I) concn, in blood plasma was detd. in the rabbit and the rat. I, when intraperitonelly injected, was rapidly absorbed into the plasma and then excreted. I concn. in plasma reached a max. lvel within 1 hour after injection, decreased gradually, and was not found after 24 hrs. The half-life of I in plasma was 1.8 hrs. When a I suspension was orally administered in doses of 200 and 100 mg/kg, the I concn. in plasma reached a max. level within 8-10 hrs., and decreased slowly. In this case, the I concn. in plasma was very low, being only 11.7 ug/ml, at the 8th hr. after the administration of 200 mg/kg. The half-life of I in plasma after its oral administration was 27 hrs. In the rat, the half0life of I in plasma was 1 hr, and 3.4 hrs, in cases of intraperitoneal and oral administrations resp. Hiroshi Kataoka.
Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire

(207)

Type: other: Bewertung der Kanzerogenität
Remark: Die Verabreichung von höheren Dosen Terephthalsäure (2 % und mehr) im Futter führt bei Ratten zur Bildung von Blasensteinen, welche hauptsächlich aus Kalziumterephthalat bestehen. Die chronische Verabreichung führt bei Ratten zu Steinen und Blasentumoren. Terephthalsäure erwies sich als nicht mutagen im Ames-Test und wird von der Ratte nicht metabolisiert, ist also vermutlich nicht gentoxisch. Die Steine verletzen die Blasenwand und verursachen Zellproliferation, was vermutlich die Hauptursache für das Auftreten von Blasenneoplasien durch Terephthalsäure ist. Da die Blasensteine erst entstehen, wenn Konzentrationen von Kalzium und Terephthalsäure im Urin das Löslichkeitsprodukt von Kalziumterephthalat überschreiten, kann ein Schwellenwert für die Bildung der Blasensteine und damit auch für die Blasentumoren festgelegt werden.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(208)

Type: other: Schwellenwert für die Bildung von Blasensteinen
Remark: Unter der Voraussetzung, daß die durchschnittlich ausgeschiedene Urinmenge beim Erwachsenen 1.5 l/Tag beträgt und daß Terephthalsäure nicht vom Menschen metabolisiert wird, müssen mindestens 2 g Terphthalsäure/Tag resorbiert werden, damit die Terephthalsäure-Konzentration im Urin hoch genug (8 mM) zur Bildung von Blasensteinen ist.
Source: Hoechst AG Frankfurt/Main
Hoechst Trevira GmbH & Co KG Frankfurt am Main

(143)

Type:
Remark: Repeated exposure.-
Oral. Doses of 1000 mg terephthalic acid/kg bw/day and above administered in the diet of rats for 90 day-2 yr have been associated with effects on the urinary tract, the bladder being most commoly involved (CIIT, 1982 & 1983; Gross, 1974; Vogin, 1972); and also increases in liver weight (CIIT, 1983). Deaths occurred at dietary levels of 5 or 10% [2500 or 5000 mg/kg bw/day] (CIIT, 1982; Haskell, 1955). In a large group of rats maintained for 2 yr on diets providing 142 mg/kg bw/day, the type and tissue abnormalities in a wide range of organs (including the urinary tract) did not differ from that seen in untreated controls (CIIT, 1983).
Source: INTERCONTINENTAL QUIMICA, S.A. MADRID

5.11 Experience with Human Exposure

Remark: The concentration of TPA that would be required to induce crystalluria or calculi in man can be computed from the solubility product. The authors described two methods to reach this value. Then assuming that in man the average urinary output is 1.54 l/day and that TPA is not metabolized, it follows that the amount of TPA that would have to be absorbed to produce an average urinary TPA concentration of 8mMol is approximately 2g/day.
Source: INCA INTERNATIONAL S.p.A. Milan
(209)

Remark: Das Auftragen einer oeligen 80 %igen Paste zeigte nach 10maliger Applikation auf die gleiche Hautstelle bei Probanden keine Reizwirkung. Ebenso wurde diese Paste nach 24 h Dauereinwirkung ohne Anzeichen einer Reizung oder Roetung vertragen.
Source: Hoechst AG Frankfurt/Main
ICI Chemicals & Polymers Limited Runcorn, Cheshire
(210)

Remark: Das Auftragen einer öligen 80 %igen Paste zeigte nach 10maliger Applikation auf die gleiche Hautstelle bei Probanden keine Reizwirkung. Ebenso wurde diese Paste nach 24 h Dauereinwirkung ohne Anzeichen einer Reizung oder Rötung vertragen.
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7.1 Risk Assessment

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