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
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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:

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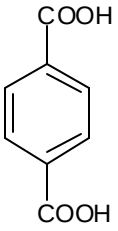
SIDS INITIAL ASSESSMENT PROFILE

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

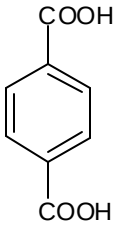
STUDY (CAS NO.: 100-21-0)		SPECIES	PROTOCOL	RESULTS
TOXICOLOGICAL DATA				
5.1	Acute Toxicity			
5.1.1	Acute oral	Rat Mouse		LD_{50} = >5000 mg/kg LD_{50} = >15380 mg/kg LD_{50} = 1960 mg/kg LD_{50} = 18800 mg/kg LD_{50} = 2000 mg/kg LD_{50} = >5000 mg/kg LD_{50} = 6400 mg/kg LD_{50} = 1470 mg/kg
5.1.2	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

Amoco Chemicals Co. (1987) Acute Inhalation Toxicity study of Purified Terephthalic Acid in Rats. Conducted by IIT Research Institute. IITRI Study #1158

Amoco Chemicals Co. (1990) Acute Dermal Toxicity Study of Terephthalic Acid in Rabbits. Test Study Reference: IITRI SN 1558, TA# 445F

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

Amoco Corporation (1970) Fifteen Week Oral Toxicity Studies of Terephthalic Acid – Albino Rats. Conducted by Toxicological Evaluations. LSL Study#1358

Amoco Corporation (1989) A Segment II Inhalation Teratology Study of Terephthalic Acid in Rats. Conducted by IIT Research Institute. IITRI Study #1448

Amoco Corporation (1990) Acute Oral Toxicity Study of Terephthalic Acid in Rats. Conducted by IIT Research Institute. IITRI Study #1557

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.

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.

Bemis, Dindorf Harwood, Samans. (1982) Kirk-Othemer Encyclopedia of Chemical Technology, 3rd Ed Vol 17, 734.

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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

CIIT (1983) Chronic Dietary Administration Of Terephthalic Acid. CIIT Docket 20124

Gerike, Fischer. (1979): Ecotoxicol. Environ. Safety 3, 159-173

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.

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

Hoshi A., Yanai R., Kuretani K. (1968) Toxicity of terephthalic acid. Chem Pharm Bull 16 1655-1660.

Kubota (1979) Ecotoxicol. Environ. Safety 3, 256-268.

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

Massman, Inst Fuer Arbeitsmedizin der Uni Tuebingen, 1966

Matsumoto (1982), Water Res. 16.

Ryan BM, Hatoum NS, Jernigan JD. (1990) A segment II inhalation teratology study of terephthalic acid in rats. Toxicologist 10, 40

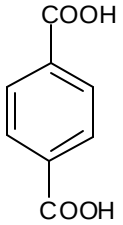
Syracuse Research Corporation calculated values SRC Report 1988

U.S. Environmental Protection Agency. (1994). Preliminary Exposure Profile: Terephthalic Acid (Draft Report).

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

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

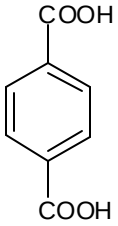
CAS NO.: 100-21-0		Information	OECD Study	GLP	Other Study	Estimation Method	Acceptable	SIDS Testing Required
STUDY		Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
PHYSICAL-CHEMICAL								N
2.1	Melting point	Y	N	N	Y	N	Y	N
2.2	Boiling point	N						N
2.3	Density	Y	N	N	Y	N	Y	N
2.4	Vapor pressure	Y	N	N	Y	N	Y	N
2.5	Partition 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^{o} 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 ^{o} C (not soluble)
Method:
GLP: Unknown
Reference: Arizona Database

Solubility: 19 mg/l at 25^{o} 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^{o} F)
Method: MicroCleveland and open cup
GLP: no
Comment: Obtained from Eastman MSDS

Flashpoint: 260^{o} 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^{o}C) of 1.19 x 10^{-5}, water solubility (20^{o}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: 5×10^5 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: 5×10^5 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 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.
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 sp ecificity 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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