# Analysis of the most appropriate risk management option (RMOA)

**Substance Name: Terephtalic Acid**

**EC Number: 202-830-0**

**CAS Number: 100-21-0**

**Authority: France**

**Date: March 2016**

**Cover Note**

*The regulatory pressure for the use of BPA has challenged the companies to find alternative solutions to polycarbonate (PC). Among the potential replacements, Polyethylene Terephthalate (PET) has emerged. Terephtalic acid is used as a monomer to make PET.*

*In the framework on the French National Strategy on Endocrine Disruptors in 2015, the French Competent Authority requested ANSES to evaluate the toxicological profile of terephtalic acid and verify whether risk management measures should be necessary for this substance.*

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# 1 IDENTITY OF THE SUBSTANCE

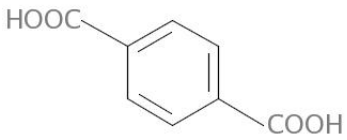
## 1.1 Other identifiers of the substance

**Table: Other Substance identifiers**

| | |
|---|---|
| **EC name (public):** | Terephthalic acid |
| **IUPAC name (public):** | Terephthalic acid |
| **Index number in Annex VI of the CLP Regulation:** | / |
| **Molecular formula:** | C8H6O4 |
| **Molecular weight or molecular weight range:** | 166 |
| **Synonyms:** | TPA |

**Type of substance** ☒ Mono-constituent ☐ Multi-constituent ☐ UVCB

**Structural formula:**



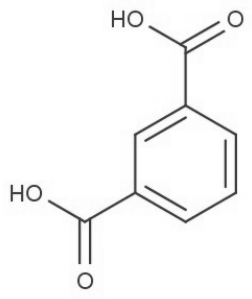

## 1.2 Similar substances / grouping possibilities

Read-across has been used in the registration dossier with isophthalic acid (CAS No 121-91-5).

**Table: Isophtalic acid**

| | |
|---|---|
| **EC number:** | 204-506-4 |
| **EC name (public):** | Isophtalic acid |
| **CAS number:** | 121-91-5 |
| **Molecular formula:** | $C_8H_6O_4$ |
| **Molecular weight or molecular weight range:** | 166 g/mol |
| **Synonyms:** | 1,3-benzenedicarboxylic acid |

**Structural formula:** *(If it is group of similar substance, give examples)*




## 2 OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

**Table: Completed or ongoing processes**

*When filling out this table and dealing with a substance for which the composition is of concern, please specify if each of the completed or ongoing processes is related to the substance as such or to the relevant constituent, impurity, additive or degradation (transformation) product/metabolite.*

| | | |
|---|---|---|
| RMOA | ☐ Risk Management Option Analysis (RMOA) other than this RMOA | |
| REACH Processes | Evaluation | ☒ Compliance check, Final decision |
| | | ☐ Testing proposal |
| | | ☐ CoRAP and Substance Evaluation |
| | Authorisation | ☐ Candidate List |
| | | ☐ Annex XIV |

| | | |
|---|---|---|
| | Restri -ction | ☐ Annex XVII[1] |
| Harmonised C&L | | ☐ Annex VI (CLP) (see section 3.1) |
| Processes under other EU legislation | | ☐ Plant Protection Products Regulation<br>Regulation (EC) No 1107/2009 |
| | | ☐ Biocidal Product Regulation<br>Regulation (EU) 528/2012 and amendments |
| Previous legislation | | ☐ Dangerous substances Directive<br>Directive 67/548/EEC (NONS) |
| | | ☐ Existing Substances Regulation<br>Regulation 793/93/EEC (RAR/RRS) |
| (UNEP) Stockholm convention (POPs Protocol) | | ☐ Assessment |
| | | ☐ In relevant Annex |
| Other processes/ EU legislation | | ☒ Other (provide further details below) |

- The decision on a compliance check required a chemical safety report ("CSR") for the registered substance, to be provided to ECHA by 29 April 2013.

- Terephtalic acid is regulated as a monomer for food contact plastics under Regulation (EU)10/2011 - on plastic materials and articles intended to come into contact with food. Terephtalic acid is a monomer of polyethylene terephthalate (PET) used as a resin for bottles, films and thermoformed packaging. The Regulation states a specific migration limit (SML) of 7.5 mg/kg.

[1] Please specify the relevant entry.

# 3 HAZARD INFORMATION (INCLUDING CLASSIFICATION)

## 3.1 Classification

### 3.1.1 Harmonised Classification in Annex VI of the CLP

There is no harmonized classification.

### 3.1.2 Self classification

- In the registration:

  The substance is not classified.

- The following hazard classes are in addition notified among the aggregated self classifications in the C&L Inventory:

  - Skin Irrit. 2 H315
  - Eye Irrit. 2 H319
  - STOT SE 3 H335 (respiratory tract)

  And for one notifier:

  - Acute Tox. 4 H302
  - Repr. 2 H361

### 3.1.3 CLP Notification Status

- *Are there CLP notifications? What is the number of aggregated notifications and the total number of notifiers?*

**Table: CLP Notifications**

| | **CLP Notifications[2]** |
|---|---|
| Number of aggregated notifications | 9 |
| Total number of notifiers | 796 |

## 3.2 Additional hazard information

**Human Health:**

Human hazards properties presented are based on available data from the chemical safety report (CSR) of Terephtalic Acid.

[2] C&L Inventory database, http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database (accessed 20 August 2015)

➢ Toxicokinetics and ADME

Terephtalic Acid (TPA) is found to be rapidly absorbed by oral route and excreted predominantly in the urine as the sulphate conjugate. In an *in vitro* study in normal and induced rat liver microsomes, no evidence of the P450-induced metabolism of terephthalic acid was observed. The weight of evidence indicates that there is little potential of bioaccumulation (Gledhill (2006), Barnes (1958), Haskell lab (1959), Wolkowski-Tyl (1982), Hoshi (1965, 1966, 1968), Anon (1984), Moffit (1975)).

➢ Acute toxicity

Oral route:

Terephthalic acid in corn oil was administered orally by gavage to male and female rats (n=5 animals/sex/dose) at dose levels of 6834, 10250 and 15380 mg/kg bw. Rats were observed for 14 days following administration. The only deaths that occurred were in the mid dose group (10250 mg/kg bw); 1 female died within 22 hours of administration, and 1 male died on day 3. Gross necropsy revealed that these rats had pale discoloured kidneys. Clinical signs observed at all dose levels included hypoactivity, ruffled fur, diarrhoea, muscular weakness and rhinitis. There were no effects on body weight gain over the 14 days. Gross necropsy of all animals surviving to the end of the 14 day observation period did not reveal any abnormalities. Therefore the acute oral LD50 is >15380 mg/kg bw (Harrison (1975)).

Inhalation route:

A study by Leach et coll. (1983) was conducted in a group of 5 male and 5 female Sprague-Dawley rats exposed to purified terephthalic Acid administered as a particulate aerosol by inhalation for two hours. The rats were exposed to an aerosol concentration of 2.02 mg/l. No rats died during the study. Therefore, the 2 hour acute inhalation LC50 of purified terephthalic acid was estimated to be greater than 2.02 mg/l. Gross necropsy revealed 1 male rat with dark lungs, and 1 male and 1 female rat with enlarged mandibular lymph nodes. No other abnormalities were detected. The 2-hour LC50 was therefore >2.02 mg/L. (Leach (1987)).

Male Fischer 344 rats were exposed to pyrotechnically disseminated terephthalic acid in nose-only exposure chambers for 30 minutes. Nominal terephthalic acid concentrations were 100, 200 and 400 mg/m$^3$. Two control groups were exposed to either air alone, or the fuse/fuel mix[3] alone. Rats underwent pulmonary function tests and bronchoalveolar lavage immediately prior to sacrifice, at 24 hours or 14 days post exposure. There were no compound-related mortalities. There were no adverse changes in pulmonary function, lavage or histopathology. The only adverse reaction observed was a dose-related rhinorrhea that disappeared within 1 hour post exposure. There was no toxic effects of the combustion byproducts (CO, $CO_2$, $NO_2$ and $SO_2$), which remained below the threshold limit value. Under the conditions of this study, the acute LC50 is greater than 235 mg/m$^3$ (analytical concentration) (Thomson (1988)).

Dermal route:

[3] Pyrotechnic dissemination : 54% terephthalic acid, 15% suger, 26% potassium chlorate, 3% magnesium chlorate, 2% nitrocellulose.

The acute dermal toxicity of terephthalic acid was determined in a limit test, with 5 male and 5 female New Zealand White rabbits (Lord (1990)). The test material was left in contact with the shaved pre-moistened skin of the rabbits, under an occlusive dressing, for 24 hours. The rabbits were observed during this time and for 14 days thereafter. No deaths occurred during the study. Mild dermal irritation (erythema) was observed within the application site of six rabbits immediately following unwrapping. Otherwise, no adverse treatment-related clinical signs were observed in any rabbits during the study. Mean body weights increased during the study. No gross pathological lesions attributable to treatment were evident in any of the rabbits at necropsy.

The acute dermal toxicity of the substance in the rabbit was found to be >2000mg/kg bw, confirming the inherently low acute dermal toxicity of the TPA.

The acute toxicity studies *via* the oral, dermal and inhalation routes indicates that TPA is of low order of toxicity and it is non-irritating to the skin and eyes (Hatoun (1990), Baker (1975a, 1975b).

- Repeated doses study

Oral route:

Terephthalic acid was fed to rats in the diet for 90 days (Vogin (1972)). The initial dose level was 5%, but this was reduced to 3% after one week into the study because the rats showed decreased body weight gain. There were no substance related mortalities. Occult blood was found in the urine, and crystalluria was seen after 90 days. There was an increase in kidney weights, but as no other organs were affected this was not thought to be biologically significant. Bladder and kidney calculi formed, with a higher incidence in males than females. The only effect noted at necropsy was a mild to moderate epithelial hyperlasia of the bladder and evidence of chronic cystitis. Default conversion factors indicate a dose level equivalent to 3000 mg/kg bw/d; using figures for food intake and final week bodyweights, intake values of 2070 and 2490 mg/kg bw/d for males and females respectively are calculated.

A study by Kohn et coll. (1970) was conducted in male and female albino rats (30 animals/sex/dose) fed to terephthalic acid for 15 weeks at dietary dose levels of 0.05, 0.16, 0.5, 1.6 and 5% (w/w). Males and females in the high dose group exhibited a small reduction in body weight gain, but food consumption and utilisation were apparently unaffected. Haematuria was observed on a sporadic basis amongst the high dose males during the second and third months of the study; haematuria was not seen in females. However, urinalysis revealed that occult blood was present at various time points in males in the 0.16, 0.5, 1.6 and 5% groups, and in females in all dose groups. It appeared that the majority of terephthalic acid was exrected in the urine. Gross pathology revealed significant effects of treatment on the urinary bladder of high dose males. A high incidence of bladder stones were found in this group, and microscopic examination revealed proliferative changes characterised by a thickening of the epithelium, and in some cases a narrowing of the lumen of the bladder was observed. It appears that males were more affected by treatment than females. The isolated findings of urinary occult blood seen at all dose levels in this study are difficult to interpret. Findings are reported semi-quantitatively (classed as 'negative', 'small', 'moderate' and 'large' for pooled urine samples taken from 2 rats/sex/group pre-test and after treatment for 1, 2 and 3 months. It is notable that the results of uirnalysis from the chronic toxicity and carcinogenicity study of Preache et al (1983) do not report any effects on the incidence of urinary occult blood (measured in 5 rats/sex at 6 and 12 months and in 20 rats /sex at 18 and 24 hours) with the exception of both sexes at the highest dose level of 1000 mg/kg

bw/day at 18 months. The effects seen at lower dose levels in the Kohn study are not considered to be reliable due to the small sample size and the potential for cross-contamination.

The 15 week dietary NOAEL could therefore be considered to be 1.6% (980 mg/kg bw/d in males, 1186 mg/kg bw/d in females).

In the study conducted by Ledoux et coll. (1982), terephthalic acid (TPA) was fed to groups of male and female Wistar and CD rats (30 animals/sex of each strain/dose) for 90 days, to investigate TPA-induced urolithiasis. Nominal dietary concentrations were 0, 0.03, 0.125, 0.5, 2.0 and 5.0%. Sacrifices were carried out at 30, 60 and 90 days for gross pathology and histopathological examination of the urinary tract. Urine was collected at the time of sacrifice. Toxicity was evident in rats fed diets containing 0.5% TPA and above; these rats exhibited reduced weight gain compared to controls. CD males fed 0.03% also exhibited significanty reduced weight gain. Five deaths occurred between 4 and 13 weeks in the rats fed 5% TPA; these rats did not have bladder calculi. Diarrhea was observed in some of the rats exposed to high TPA concentrations. A small number of bladder calculi were found in rats fed the 5% TPA-diet for 90 days; calculi were more frequently observed in Wistar rats (6/20) than CD rats (1/20). TPA-administration resulted in a decrease in urinary pH. Chronic inflammatory lesions of the bladder and urethra were observed in treated rats, with the highest incidence occurring in rats fed 5% TPA. Nodules and cysts containing parasitic larvae were discovered in the liver of a number of treated rats. Some small strain differences were present, but it was concluded that there is no substantial difference in TPA toxicity between CD and Wistar rats. Based on body weight reductions, the NOAEL can be considered to be 0.125% TPA in the diet.

In study of Williams (1955) conducted in male and female albino rats (6 animals /sex/dose) fed with terephthalic acid in the diet for 90 days, at levels of 0, 1, 3.2 and 10%. All groups showed a tendency towards anaemia. Pathological examination of the 3.2% group revealed mild injury to the urinary tract in 2 of 12 rats. Rats fed 10% showed decreased food consumption and growth rate, and exhibited recurring haematuria. Males were more affected than females. Pathological examination revealed the presence of calculi in the urinary tract. A NOAEL of 1% (approximatley equivalent to 1000 mg/kg bw/d) can be determined for this study, however it is noted that the investigations in this study were limited.

Inhalation route:

In a supportive study (Leach (1987), terephthalic acid was administered as an aerosol by inhalation at target concentrations of 0, 0.5, 1.0 and 3.0 mg/m³ to four groups of 10 male and 10 female Sprague-Dawley rats each. The rats were exposed 6 hours per day, 5 days per week, for 4 weeks. There were no statistically significant effects of treatment on body weights, organ weights, haematology or clinical chemistry parameters. Pulmonary function assessments did not reveal any significant differences between the control and high exposure groups. A NOAEC could not be identified due to histopathological evidence of tracheal irritation in all exposure groups; the lowest exposure concentration of 0.5 mg/m³ can be considered a minimal LOAEC.

In a GLP compliant study by Fuhst (2008), the objective was to evaluate the possible toxicity of terephthalic acid after inhalation in rats for 28 days. Fifty male and fifty female Sprague Dawley rats (Crl:CD(SD)), approximately 8 weeks of age at study start were exposed for 6 hrs/day, 5 days/week over a period of 4 weeks to clean air or terephthalic acid at concentrations of 1.03 mg/m³, 2.93 mg/m³ and 10.05 mg/m³ for the low, medium, and high dose group. The mass

aerodynamic diameter (MMAD) was 3.25, 2.87, and 2.94 µm for the low, medium, and high dose group. Additionally the study included a control and high dose group with a 14 day recovery period. In addition the effect (degeneration of the tracheal lining epithelium) observed in the previous 28-day study performed by the IIT Research Institute (Leach & Hatoum, 1987) was investigated. No significant inflammatory or other lesions were observed in the terephthalic acid treatment groups under the present experimental conditions.

Via inhalation, the 2 studies available are contradictory. Without access to the study reports, it is difficult to understand such divergence.

The primary adverse effects of high doses of TPA to rats is almost completely restricted to the urinary tract. These effects include formation of bladder calculi, and inflammatory changes, hyperplasia of the bladder epithelium. At dose greater than 2% (>100 mg/kg bw/d), rats treated for two years developed bladder calculi, bladder hyperplasia and bladder tumors.

- Skin irritation and corrosion

The data reported here are those found on ECHA website with no further detail. It is reported that terephthalic acid was applied for 4 hours to the shaved backs of 3 rabbits at a dose of 0.5 g. Following unwrapping, the test sites were rinsed with saline. All test sites were examined for signs of irritation and corrosivity according to the Draize method at 30-60 minutes, 24, 48 and 72 hours following removal of the wrappings. No signs of dermal corrosivity were seen in any rabbit during the study. The irritation score ranged from 0.7/8.0 at 30-60 minutes, to 0.0/8.0 at 72 hours following unwrapping. The Primary Dermal Irritation Score for terephthalic acid was 0.2. It can be concluded that terephthalic acid is not irritating to rabbit skin. This result is not coherent with some self-classification on terephtalic acid irritating properties.

- Eye irritation and corrosion

100 mg undiluted terephthalic acid was instilled into one eye of 6 albino rabbits and ocular reactions assessd for up to 7 days. Effects were limited to grade 1 conjunctival erythema and chemosis in all rabbit, with grade 1 corneal opacity also apparent in 1 rabbit at 24 hours only. Conjunctival discharge was additionally noted in 1 rabbit at 24 hours only. The substance is a mild eye irritant.

- Sensitization

No data are available for terephthalic acid, however a negative Buehler study was reported for the read across substance isophthalic acid.

- *In vitro* and *in vivo* genotoxicity

Six keys *in vitro* studies are available. In one Ames test (Dupont (1979) using a method similar to OECD 471, terephthalic acid was tested in Salmonella typhimurium strains TA 1535, TA 1537, TA 98 and TA 100. This chemical is not mutagenic for these strains of bacteria in the presence or absence of an activation system. In four chromosomal aberration assay (Fox (2006a, 2006b, 2006c, 2007a, 2007b)) which followed guidelines similar to OECD 473 no structural damage was induced in lymphocytes exposed to TPA (terephtalic acid) by oral route.

In one mammalian cell gene mutation assay (Riach and Willington (1994) which followed guidelines OECD 476, no data are available for terephthalic acid,

however a negative result was reported for the read across substance isophthalic acid.

Two *in vivo* key study (Gudi (2001) are avalaible. In one micronucleus assay, terephthalic acid was administered i.p. at doses of 0, 200, 400 and 800 mg/kg. Bone marrow cells were harvested 24 or 48 hours later. The positive control was cyclophosphamide. No significant increase in micronucleated polychromatic erythrocytes in test article treated groups relative to vehicle controls was observed. Under the conditions of this study, the results are negative in the mouse micronucleus test. In one *in vivo* key study (Fox, (2006c)), purified terephthalic acid was tested for the indication of unscheduled DNA synthesis (UDS) in rat liver *in vivo* at the limit dose of 2000 mg/kg bw. The data from the study do not indicate any DNA repair induced in the rat liver following treatment with purified terephthalic acid.

TPA is considered to be non-genotoxic in regards to clearly negative studies *in vivo* (Gudi (2001), Fox (2006c), Lee (2007), Ball (2012)) and no evidence of genotoxicity seen in Ames test (Dupont (1979), *in vitro* aberration chromosomes tests (Fox (2006a, 2006b, 2006c, 2007a, 2007b)) and by read across using isophthalic acid in mammalian cell gene mutation assay (Riach and Willington 1994).

- Carcinogenicity

In a study conducted by Gross (1974), groups of 50 Wag/Rij Wistar-strain rats per sex were fed a basal diet or the diet incorporating 1, 2, or 5% terephthalic acid (97.3% purity) for two years. These doses correspond to 500, 1000, or 2500 mg/kg bw/d. Clinical observations were made daily, and animals were weighed weekly for the first three months and then bi-weekly. The author concluded that the presence of stones changed the urinary tract epithelium resulting in hyperplasia, papilloma, squamous metaplasia and further to both transitional cell tumors or squamous cell carcinoma, and further that 1% (500 mg/kg bw/d) dietary terephthalic acid had no demonstrable toxicity for Wistar rats under the conditions of this study.

In another study (Preache, 1983) male and female Fischer 344 rats (126 rats/sex/dose) were fed terephthalic in the diet at concentrations of 0, 20, 142 or 1000 mg/kg/day to determine any toxic/carcinogenic effects. Bladder transitional cell adenomas and a single carcinoma were present in female rats at the high dose level; findings were associated with diffuse epithelial hyperplasia. The result shows the evidence of bladder carcinogenicity was seen in females at the highest dose level in this study.

In the study conducted by Ackerman (1983), terephthalic acid was evaluated for chronic toxic and carcinogenic effects in male and female Fischer 344 rats (126 rats/sex/group) following dietary administration at levels of 0 (basal diet only), 20, 142 or 1000 mg/kg bw/d. Growth was retarded in a dose-related manner for female rats fed diets containing terephthalic acid at doses of 1000, 142, or 20 mg/kg/day. The effects at the lower dose were of shorter duration with recovery evident after approximately 6 months. The highest dose of terephthalic acid also retarded growth in male rats. Urotithiasis was induced in female rats fed 1000 mg/kg/day terephthalic acid but not in male rats nor in females fed the lower doses. The high dose of terephthalic acid also induced transitional cell tumors and squamous metaplasia in the bladder of females and may have increased the incidence of bladder hyperplasia. At the terminal sacrifice, a reduction in urine pH was observed in males fed the high dose of terephthalic acid and there were slight increases in water consumption for this group at the terminal sacrifice and for the high dose females at the 18 month sacrifice. Alterations in organ weights were observed at various periods of the study and especially at study termination

in males and females in the high dose groups. However, except for an increase in relative liver weight, these were generally consistent with overall reductions in body weight. Survival may have been altered by feeding of terephthalic acid to female rats but this was not evident prior to final period of the study (18-24 months) and was not dose related.

EPA (1984) reviewed the available literature and concludes that low levels (<1%) of terephthalic acid do not seem to induce carcinogenic effects. However, at 5% terephthalic acid formation of bladder and ureteral neoplasms were noted in male and female rats.

In conclusion, evidence of carcinogenicity was seen in a chronic rat study in which female rats had an increased incidence of bladder transitional cell adenomas and carcinomas at the highest dose level equivalent to approximately 1000 mg/kg/bw/d (Preache (1983), Ackerman (1983), EPA (1984), Gross (1974)). Toxicity is associated with urolithiasis which is characterized by calculus formation and urinary sediment. Studies have demonstrated that stones are formed largely of calcium terephthalate due to pH dependent-precipitation of urinary calcium terephthalate at concentrations level exceeding the limits of solubility. 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.

Moreover, the bladder effects found in most of the studies are most probably linked to irritating property of terephthalic acid and therefore not judged as apical finding to be considered for ED evaluation. Moreover, Humans are generally considered to be less sensitive than rats to urolithiasis for anatomical reasons. It is possible that urolithiasis could occur in exposed humans; however it extremely unlikely that humans could be exposed to the levels of TPA of the magnitude used in the rat toxicity studies, or for similarly long periods.

- Reproductive and developmental toxicity

TPA is not a reproductive or developemental toxicant.

No evidence of developmental toxicity was seen in an inhalation study in rats exposed during GD6 to GD15 to TPA at levels of up to 10 $mg/m^{-3}$ (Ryan (1990)).

In a two generation study, a groups of 26 male and 26 female (F0) parents) weanling Alpk:APfSD (Wistar-derived) rats were fed diet containing 0 (control), 1000, 5000 or 20000 ppm terephthalic acid. After 10 weeks, the animals were mated and allowed to rear the ensuing Fl litters to weaning. The breeding programme was repeated with the Fl parents selected from the Fl pups to produce the F2 litters after a 10-week pre-mating period. Test diets were fed continuously throughout the study. The growth of the parental generation, reproductive function, mating behaviour, conception, gestation, parturition, lactation and weaning and the growth and development of the pup were determined. These results does not report any evidence of reproductive toxicity (including sperm parameters) in rats administered TPA at levels of up to 20,000 ppm (2010.9-2323.3 mg/Kg bw/d) in the diet (Milburn (2003a, 2003b, 2003c, 2003d), Jacobsen (2003).

Concerning endocrine disrupter's (ED) properties of TPA, there are no particular ED concerns due to the lack of specific methodology to investigate ED endpoints.

On the Cui *et al* (2004) study, rats received terephthalic acid 0, 0.2, 1 and 5% in the diets for 90 days, and sacrificed on the 91st day. Daily sperm production was measured , sperm motility was assessed by means of computer-assisted sperm analysis (CASA) and serum testostone was measured by radioimmunoassay. The

male fertility study the effects of terephthalic acid on some rat sperm motility parameters did show dose-response and no NOAEL was identified. However, the study is difficult to interpret due to lack of information regarding the methodology and statistics. The study shows weaknesses on the methodological description about analysis of the sperm movement. The results are obtained using a time of acquisition too short for analysed the movement of sperm cells. The statistical methodology is poorly described, so in front of these methodological and statistical limits, it is difficult to conclude.

- Neurotoxicity

There is no indication of neurotoxicity from the standard toxicity studies.

- Immunotoxicity

There is no indication immunotoxicity from the standard toxicity studies.

**Environment:**

Hazards properties presented are based on available data from the CSR of Terephtalic Acid. This substance was also reviewed under the OECD Cooperative Chemicals Assessment Programme (SIAM 12, 2001).

- E-fate of TPA

Terephtalic Acid (TPA) is a solid with a melting point of ca. 400 °C; under normal conditions TPA will therefore undergo direct transition from the solid to the vapor phase without melting. TPA has low water solubility in the range of 17 to 19 mg/L (25 °C), and has a negligible volatility vapor pressure 0.00158 Pa (25 °C). TPA is unlikely to partition from aqueous systems to the atmosphere (Henry's Law Constant = 3.9.10-8 Pa $m^3$/mol, HENRYWIN v3.20). The pKa values in aqueous solution at 25 °C are 3.54 and 4.46. The measured log Kow is determined to be 2.

If released to air, terephthalic acid will exist solely in the particulate phase in the atmosphere. TPA absorbs UV light at wavelengths >290 nm, and therefore may be susceptible to direct photolysis by sunlight. TPA is expected to undergo atmospheric oxidation in air with an estimated half-life of about 13 days.

If release into water, terephthalic acid is not expected to volatilize from water surfaces nor to hydrolyze in the environment due to the lack of functional groups that hydrolyze under environmental conditions.

Using a wide variety of methods and terephthalic acid concentrations, screening tests report that TPA is readily biodegradable: coupled Units (93% DOC, 1-day), Zahn-Wellens (93% DOC,4-days), Sturm Test (72% CO2 evolution, 28 days), Modified OECD Test (82% DOC, 19-day surface water die-away) and Closed Bottle Test (112% BODT, 30 days).

The estimated log Koc of TPA is between 18 to 79 L/Kg, then it is not expected to adsorb to suspended solids and sediment and has high mobility in soil. TPA has low potential for bioaccumulation (estimated BCF = 3.16).

The low pKa values indicate that TPA will rapidly be converted to salts under environmental conditions. Furthermore, process effluents will be pH-balanced prior to treatment to protect both the plant infrastructure from corrosion and the biological treatment process from pH shock effects. Then, the more environmentally relevant forms to be discharged are terephthalate salts that are

more highly water soluble, and which have a correspondingly lower Koc and kow than that of the free acid.

- Ecotoxicity of TPA

The toxicity of TPA on aquatic species is low. Reliable experimental results from tests on fish, daphnia, and algae are available. According to OECD SIDS, the lowest reliable acute toxicity values for the sodium terephthalate salts are:

- for fish: 96h-$LC_{50}$ ranged from greater than 500 to 1640 mg/L;
- for invertebrates (*Daphnia*): 48h $EC_{50} \geq 982$ mg/L;
- for algae (*S. subspicatus*): NOEC > 1000 mg/L.

Using the lowest reported $LC_{50}$ value, a $PNEC_{surface\ water}$ derived in the OECD SIDS is equal to 8 mg/L.

No relevant toxicity data on sediment and terrestrial organisms are available to derive the $PNEC_{sed}$ and the $PNEC_{soil}$.

- PBT assessment

TPA is readily biodegradable according to the results of standard tests, therefore does not fulfil the persistent (P) criteria. The calculated BCF of Terephthalic acid is 3.16 L/kg wet weight and below the threshold value of 2000. Terephthalic acid does not fulfil the bioaccumulation (B) criteria. The long-term NOECs for freshwater algae and invertebrates are 19.0 and 19.5 mg/L, respectively, for the free acid form of TPA. Both values exceed the trigger value of 0.01 mg/L. TPA does not satisfy the environmental effects criterion for classification as toxic (T).

Terephthalic acid is therefore not a PBT (or vPvB) substance.

- Endocrine disruptor characteristic of TPA for the environment

There is no literature data on potential endocrine effects on the environmental organisms.

# 4 INFORMATION ON (AGGREGATED) TONNAGE AND USES[4]

## 4.1 Tonnage and registration status

**Table: Tonnage and registration status**

| **From ECHA dissemination site** | | |
|---|---|---|
| ☐ Full registration(s) (Art. 10) | ☐ Intermediate registration(s) (Art. 17 and/or 18) | |
| Tonnage band (as per dissemination site) | | |
| ☐ 1 – 10 tpa | ☐ 10 – 100 tpa | ☐ 100 – 1000 tpa |
| ☐ 1000 – 10,000 tpa | ☐ 10,000 – 100,000 tpa | ☐ 100,000 – 1,000,000 tpa |
| ☒ 1,000,000 – 10,000,000 tpa | ☐ 10,000,000 – 100,000,000 tpa | ☐ > 100,000,000 tpa |
| ☐ <1 . . . . . >+ tpa (e.g. 10+ ; 100+ ; 10,000+ tpa) | | ☐ Confidential |
| *Joint Submission* | | |

## 4.2 Overview of uses

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. 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 polybutylene terephthalate engineering resins used primarily in automobile parts (OECD SIDS 2001).

Polyethylene terephthalate (PET) is a linear polyester produced by polycondensing of ethylene glycol and terephthalic acid. It can replace the polycarbonate in bottles and food containers (Anses, 2013). PET is used for soft drink bottles because of its impermeability to $CO_2$.

[4] *Please provide here the date when the dissemination site was accessed.*

It should be noted that this polymer has been positively evaluated by the US FDA: Food Contact Notification ( FCN ) No 85 for use as films or articles intended to be in contact with aqueous food products, acids, fatty and with low alcohol.

The following information is extracted from the ECHA dissemination website (consulted the 20 August 2015):

**Table: Uses**

| | **Use(s)** |
|---|---|
| **Uses as intermediate** | Industrial manufature of polymers |
| **Formulation** | Industrial manufature of polymers<br>Industrial manufacture of esters<br>Rubber production and processing<br>PET polymer production |
| **Uses at industrial sites** | Industrial manufature of polymers<br>Industrial manufacture of esters<br>Laboratory chemicals<br>Use as a fuel<br>Functional fluids |
| **Uses by professional workers** | Laboratory Chemicals<br>Polymer<br>Use as a fuel<br>Functional fluids |
| **Consumer Uses** | Polymer<br>Use as a fuel |
| **Article service life** | Polymer: Polyester<br>PET polymer production<br>Articles made of polymer based on PTA |

Uses advised against:

Uses at industrial Sites: Firework applications.

## 4.3 Additional information

- Uses and potential for exposure

Terephthalic acid is primarily used in the manufacture and production of polyester fibers, films, polyethylene terephthalate solid-state resins and polyethylene terephthalate engineering resins. Manufacture of polyester fibers accounts for a majority of terephthalic acid use. Polyethylene terephthalate 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 (OECD SIDS 2001).

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. According to OECD, 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. Many migration tests of PET monomers into distilled water are conducted every year worldwide as part of necessary compliance, the migration of monomers including TPA from PET into distilled water is so low that the results are never published because the lack of practical interest (Bach 2011).

'The Polyester Monomers Consortium' (PMC) in conjunction with 'The Committee of PET Manufacturers' (CPME) in Europe supplied Anses anonymised data, which aim to demonstrate that there is no detectable migration of PTA from PET food contact containers into liquid for human consumption.

In a series of separate and independent analyses (6 results), PET bottle samples were tested for 10 days at 60°C by total immersion into solutions of 3% acetic acid, 10% (v/v) aqueous ethanol, 20% (v/v) aqueous ethanol, 50% (v/v) aqueous ethanol 95% (v/v) aqueous ethanol, and olive oil for specific migration testing for terephthalic acid, Isophthalic acid and ethylene glycol. PTA extracts were determined using high-pressure liquid chromatography (HPLC). It was concluded that the migration of PTA from PET is negligible. In the specific migration analysis detailed in this paper, it can be seen that the limit of detection at various laboratories across Europe is getting lower. Even at these very low detection limits, no PTA migration could be measured (see results in Annex I).

In addition to laboratory measurement data, there are predictive models for migration of terephthalic acid from PET polymer: this recent review of the data indicated that the specific migration of PET monomers like terephthalic acid is negligible under storage conditions (Welle, 2014).

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 according to OECD SIDS 2001. As the substance is not classified in the registration, no exposure scenarios are provided in the CSR according to REACH Guidance. There are therefore no exposure estimates to ascertain this hypothesis.

However limited occupational data provided by 2 companies are reported in Annex I.

- <u>Risk for the Environment</u>

Exposure assessment and risk characterisation have not been proposed by the registrant. Very few monitoring data are available. Detection of terephthalic acid in air and water samples has been in the low ppt range: the maximum concentration of TPA in river water in Japan was 3.4 mg/L; it was detected at a concentration of 5.3 ppb in the effluent of night soil treatment plant in Japan. Environmental monitoring data in European sites are not available. Terephthalic acid is expected to partition to water and soil, where it will biodegrade and not persist or bioaccumulate. The pKa values indicate that this compound will principally exist in anion form in the environment and anions generally do not adsorb more strongly to soils containing organic carbon and clay than their neutral counterparts. If released into water, terephthalic acid is not expected to adsorb to suspended solids and sediment based upon the estimated Koc. Finally, TPA is non-toxic to aquatic organisms at concentration lower than its water solubility (between 17 to 19 mg/L). Consequently, terephtalic acid is of low priority for further work.

# 5 JUSTIFICATION FOR NO FURTHER ACTION

The presently available information indicates that terephalic acid (TPA) is not expected to pose any health or environmental risks exept irritation does appear in different tissues depending on the route of exposure. Similar conclusions were made for DEHTP (parent substance, CAS No 6422-86-2).

Regarding endocrine disruption, 2 Member States experts agreed with France's conclusions based on the current available data (following ED Expert Group discussions the 2-3 September 2015): terephthalic acid is not considered as a reproductive or developemental toxicant and no alert was found on potential endocrine disruption properties.

Given that a multi-generation rat studiy have been submitted and show limited effects and irritative bladder effects also seen in other sub-chronic and chronic studies it is difficult to suggest this substance has a reproductive effect. Moreover,the bladder effects found in most of the studies are probably linked to irritating property of terephthalic acid and therefore not judged as apical finding to be considered for ED evaluation. Humans are generally considered to be less sensitive than rats to urolithiasis for anatomical reasons. It is possible that urolithiasis could occur in exposed humans; however it is extremely unlikely that humans could be exposed to the levels of TPA of the magnitude used in the rat toxicity studies, or for similarly long periods.

It is not possible to conclude on the endocrine disruptor character of terephthalic acid because there is no solid information on the other ED effects such as Androgen or thyroid transactivation or steroidogenesis in vitro (OECD TG 456). Furthermore some uncertainties remain: Anses' ED Expert Group concluded that the study Cui et al., 2004 misses some key parameters in sperm quality analysis and it is difficult to interpret some of the other parameters.

Considering the environmental fate and (eco)toxicity properties of TPA, and in accordance with the SIDS (SIAM 12, June 2001), no further work is recommended for this substance. This conclusion is supported by migration data showing a low potential to expose consumers from PET.

The irritating property observed in vivo via inhalation (Leach, 1987) xxx are in line with some self-classification (>20%). As this is not a priority endpoint, ANSES advise the registrant notifying irritant properties to submit a proposal or to discuss for an harmonization of the self-classifications.

# 6 REFERENCES

Ackerman, L. J. (1983). Chronic dietary administration of terephthalic acid (revised pathology report). Experimental Pathology Laboratories, Inc., CIIT Project Number L-8026. Testing laboratory: Experimental Pathology Laboratories, Inc. Report no.: L-8026. Owner company: Chemical Industry Institute of Toxicology, Research Triangle Park. Report date: 1983-11-23.

Anses. Substitution du bisphénol A. Rapport d'étude. Mars 2013 [in French].

Bach C et coll. Chemical compounds and toxicological assessments of drinking water stored in polyethylene terephthalate (PET) bottles: A source of controversy reviewed. Water research 46 (2012) 571-583.

Anon. (1984). Health and Environmental Effects Profile for Terephthalic Acid. Health and Environmental Effects Profile for Terephthalic Acid, Environmental Criteria and Assessment Office, Office of Research and Development, U. S. Environmental Protection Agency. Testing laboratory: U. S. Environmental Protection Agency. Report no.: EPA-600/X-84-109.

Baker, R. G. (1975a). Primary skin irritation test - albino rabbits. Industrial BIO-Test Laboratories, Inc. Baker (1975). IBT No.: 601-06339. Testing laboratory: Industrial BIO-Test Laboratories, Inc. Report no.: IBT No.: 601-06339. Owner company: BP. Report date: 1975-03-14.

Baker, R. G. (1975b). Eye Irritation Test - Albino Rabbits. Industrial BIO-Test Laboratories, Inc. Baker (1975) IBT No. 601-06339. Testing laboratory: Industrial BIO-Test Laboratories, Inc. Report no.: IBT No. 601-06339. Owner company: BP. Report date: 1975-03-17.

Ball et coll. Toxicological review and oral risk assessment of terephthalic acid (TPA) and its esters: A category approach. Crit Rev Toxicol. 2012 Jan;42(1):28-67.

Barnes, J. R. (1958). Absorption and Excretion of Terephthalic Acid, its Sodium Salt and Methyl ester by the Rat. Testing laboratory: DuPont. Report no.: 55-58. Owner company: DuPont.

Cui, L., Dai, G., Xu, L., Wang, S., Song, L., Zhao, R., Xiao, H., Zhou, J., Wang, X. (2004). Effect of oral administration of terephthalic acid on testicular functions of rats. Toxicology, 201: 59-66. Publ.: Elsevier.

Cui L et coll. Modification of N-Methyl-N-Nitrosourea initiated bladder carcinogenesis in Wistar rats by terephthalic acid. Toxicol Appl Pharmacol. 2006 Jan 1;210(1-2):24-31.

DuPont (1979). Mutagenic Activity in the Salmonella/Microsme Assay. Testing laboratory: Haskell Laboratory report. Report no.: 148-79. Owner company: DuPont.

EPA (1984). Health and Environmental Effects Profile for Terephthalic Acid. Health and Environmental Effects Profile for Terephthalic Acid, Environmental Criteria and Assessment Office, Office of Research and Development, U. S. Environmental

Protection Agency. Testing laboratory: U. S. Environmental Protection Agency. Report no.: EPA-600/X-84-109.

Food Law Compliance of Poly(ethylene Terephthalate) (PET) Food Packaging Materials, Frank Welle, Food Additives and Packaging, Chapter 16, pp 167–195 Chapter DOI: 10.1021/bk-2014-1162.ch016, ACS Symposium Series, Vol. 1162 ISBN13: 9780841230248eISBN: 9780841230255, Publication Date (Web): July 22, 2014.

Fox, V. (2006a). Terephthalic Acid: In Vitro Cytogenetic Assay in Human Lymphocytes. Testing laboratory: Central Toxicology Laboratory. Report no.: SV1255. Owner company: BP.

Fox, V. (2006b). Sodium Terephthalate: In vitro Cytogenetic Assay in Human Lymphocytes. Testing laboratory: Syngenta, Central Toxicology Laboratory. Report no.: SV1318-TEC. Owner company: BP.

Fox, V. (2006c). Purified Terephthalic Acid: In vivo rat liver unscheduled DNA synthesis assay. Testing laboratory: Central Toxicology Laboratory. Report no.: SR1302. Owner company: BP.

Fox, V. (2007a). Additional chromosome aberration analysis of slides from an in vitro cytogenetic study on sodium terephthalate. Testing laboratory: Syngenta, Central Toxicology Laboratory. Report no.: SV1380. Owner company: BP.

Fox, V. (2007b). Sodium Terephthalate-Bridging Report to Combine the Data of an In Vitro Cytogenetic Assay in Human Lymphocytes and Additional Analysis of these Slides. Testing laboratory: Syngenta, Central Toxicology Laboratories. Report no.: SV1386. Owner company: BP.

Fuhst, R. (2008). 28-Day Inhalation Toxicity Study of Terephthalic Acid in Sprague Dawley (SD) Rats. Fraunhofer ITEM Study No. 02G06019. Testing laboratory: Fraunhofer Institute of Toxicology and Experimental Medicine, Germany. Report no.: 02G06019. Owner company: PlasticsEurope. Report date: 2009-09-30.

Gledhill, A. (2006). Terephthalic Acid: Mouse Metabolism Study. Testing laboratory: Central Toxicology Laboratory. Report no.: UM0853. Owner company: BP.

Gross J (1974). The effects of prolonged feeding of terephthalic acid (TPA) to rats. U. S. Department of Agriculture, Agriculture Research Service, Foreign Research and Technical Program Division, Washington D. C. Report no.: Project FG-Is-175.

Gudi, R., Krsmanovic, L. (2001). Mammalian Erythrocyte Micronucleus Test. BioReliance, Study No. AA41MJ.123. BTL. Testing laboratory: BioReliance, Rockville, MD. Report no.: AA41MJ.123. BTL. Owner company: BP. Report date: 2001-06-07.

Harrison, W. A. (1975). Acute oral toxicity study - albino rats. Industrial BIO-test Laboratories Inc. (Harrison, 1975). IBT no. 601-06339. Testing laboratory: Industrial BIO-test Laboratories Inc. Owner company: BP. Report date: 1975-03-17.

Haskell Laboratory (1959). Excretion of terephthalic acid by the rat: Haskell Laboratory, Medical Research Project no. MR-495-1, Report no. 8-59. Testing

laboratory: Haskell Laboratory for Toxicology and Industrial Medicine. Report no.: 8-59. Owner company: DuPont. Report date: 1959-04-21.

Hatoum, N. & Goon, D. (1990). Abbreviated Acute Dermal Irritancy/Corrosivity Study of Terephthalic Acid in Rabbits. Testing laboratory: IIT Research Institute, Life Sciences Research, Chicago. Report no.: 10820-97. Owner company: BP. Study number: 1556. Report date: 1990-11¬04.

Hoshi, A., & Kuretani, K. (1965). Metabolism of Terephthalic Acid (I) Excretion of Terephthalic Acid in Urine. Yakugaku Zasshi 85(10): 905-908.

Hoshi, A., & Kuretani, K. (1968). Distribution of Terephthalic Acid in Tissues. Chemical and Pharmaceutical Bulletin 16(1): 131-135.

Hoshi, A., Takagi, J., Yanai, R., Kuretani., K. (1966). Metabolism of Terephthalic Acid (II) Plasma Concentration of Terephthalic Acid and Its Biological Half-Life. Yakugaku Zasshi, 86(10): 963¬967.

Jacobsen, M. (2003). Terephthalic Acid: Multigeneration Reproduction Toxicity Study in Rats; Pathology Comment on the Renal Findings from study RR0915. Testing laboratory: Central Toxicology Laboratory. Owner company: BP.

Kohn, F. E., Stahoviak, E. F., Vega, S. M. (1970). Fifteen week subacute oral toxicity of terephthalic acid - albino rats. Lifestream Laboratories Project Number 1358. Testing laboratory: Lifestream Laboratories, Toxicological Evaluations, Illinois. Report no.: 1358. Owner company: BP. Report date: 1970-05-26.

Leach, C. & Hatoum, N. (1987). Four-Week Inhalation Toxicity Study of Terephthalic Acid in Rats Addendum to Final Report. Testing laboratory: IIT Research Institute, Life Sciences Research, Chicago. Report no.: L8100. Owner company: BP. Study number: 1104. Report date: 1987-12-07.

Ledoux TA, Reel JR & Gralla EJ (1982). A Ninety-Day Study of Terephthalic Acid-(CAS. No. 100-21-0) Induced Urolithiasis and Reproductive Performance in Wistar and CD Rats. Testing laboratory: Chemistry and Life Sciences Group & Chemical Industry Institute of Toxicology, Research Triangle Institute, USA. Report no.: RTI/1937/00-04F. Study number: CIIT Docket # 11622. Report date: 1982-02-15.

Lee KH, Lee BM. (2007). Study of mutagenicities of phthalic acid and terephthalic acid using in vitro and in vivo genotoxicity tests. J Toxicol Environ Health Part A 70:1329–1335.

Lord, C. (1990). Acute dermal toxicity study of terephthalic acid in rabbits. Testing laboratory: IIT Research Institute, Life Sciences Research, Chicago. Report no.: L08100. Owner company: BP. Study number: 1558. Report date: 1990-07-06.

Luciani-Torres M et coll. Exposure to the polyester PET precursor—terephthalic acid induces and perpetuates DNA damage-harboring non-malignant human breast cells. Carcinogenesis vol.36 no.1 pp.168–176, 2015

Milburn, G. M. (2003a). Terephthalic acid: Multigeneration Reproduction Toxicity Study in Rats. Testing laboratory: Central Toxicology Laboratory. Report no.: RR0915. Owner company: BP.

Milburn, G. M. (2003b). Terephthalic Acid: Multigeneration Reproduction Toxicity Study in rats Volume II of IV. Testing laboratory: Central Toxicology Laboratory. Report no.: RR0915. Owner company: BP.

Milburn, G. M. (2003c). Terephthalic Acid: Multigeneration Reproduction Toxicity Study in Rats Volume III of IV. Testing laboratory: Central Toxicology Laboratory. Report no.: RR0915. Owner company: BP.
Milburn, G. M. (2003d). Terephthalic Acid: Multigeneration Reproduction Toxicity Study in Rats Volume IV of IV. Testing laboratory: Central Toxicology Laboratory. Report no.: RR0915. Owner company: BP.

Moffitt AE Jr, Clary JJ, Lewis TR, Blanck MD, Perone VB. (1975). Absorption, distribution and excretion of terephthalic acid and dimethyl terephthalate. American Industrial Hygiene Association Journal 1975 Aug;36(8):633-41. Publ.: Taylor & Francis.

OECD SIDS Initial Assessment Report. Terephtalic Acid (TPA). June 2001.

Preache MM (1983). Chronic dietary administration of terephthalic acid. IIT Research Institute, Life Sciences Division, Report No. IITRI-L8026-6A, CIIT Docket #20124. Testing laboratory: Life Sciences Division, IIT Research Institute, Chicago, USA. Report no.: IITRI-L8026-6A. Owner
company: CIIT, Research Triangle Park, North Carolina, USA. Study number: CIIT Docket #20124. Report date: 1983-12-01.

Riach CG & Willington SE (1994). P. I. A. Purified Isophthalic Acid Mouse Lymphoma Mutation Assay. Unpublished. Testing laboratory: Inveresk Research International. Report no.: 10560. Owner company: Flint Hills Resources. Report date: 1994-12-22.

Ryan, B. M., Hatoum, N. S., Jernigan, J. D. (1990). A segment II inhalation teratology study of terephthalic acid in rats. Toxicologist 10(1): 40 (abstract 159).

Thomson, S. A., Burnett, D. C., Crouse, C. L., Hilaski, R. J., Muse, W. T. (1988). Acute Inhalation Toxicity of Pyrotechnically Disseminated Terephthalic Acid. Chemical Research, Development & Engineering Center, CRDEC-TR-88134. Testing laboratory: Chemical Research, Development & Engineering Center, Aberdeen Proving Ground, MD. Report no.: CRDEC-TR-88134. Owner company: US Army Armament Munitions Chemical Command. Study number: 1L162622. Report date: 1988-07-01.

Vogin EE (1972). Subacute feeding studies (13-week) in rats with Dimethylterephthalate (DMT), Isopthalic Acid (IA), and Terephthalic Acid (TA). Food and Drug Research Laboratories Incorporated, New York. Laboratory No. 0411. Testing laboratory: Food and Drug Research Laboratories Incorporated, New York. Report no.: 0411. Owner company: BP. Report date: 197203-30.

Williams JW (1955). 90-Day feeding tests with terephthalic acid and ethylene glycol-terephthalic acid resin. Haskell Laboratory, HL-81-55. Testing laboratory: Haskell Laboratory for Toxicology and Industrial Medicine. Report no.: HL-81-55. Owner company: DuPont. Report date: 1955-08-17.

Wolkowski-Tyl, R., Chin, T. Y., Heck, D'A. (1982). Chemical Urolithiasis III. Pharmacokinetics and Transplacental Transport of Terephthalic Acid in Fischer-344 Rats. Drug Metabolism and Disposition, 10(5): 486-490.