Triethyl phosphite
CAS No: 122-52-1
SID Initial Assessment Report

For

SIAM 16

Paris, France, 27 – 30 May 2003

1. Chemical Name: Triethyl phosphite
2. CAS Number: 122-52-1
3. Sponsor Country: Germany
   Contact Point:
   BMU (Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit)
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4. Shared Partnership with:

5. Roles/Responsibilities of the Partners:
   - Name of industry sponsor /consortium: Bayer AG, Germany
     Contact person: Dr. Burkhardt Stock
     Gebäu.de 9115
     D-51368 Leverkusen
   - Process used: See next page

6. Sponsorship History
   - How was the chemical or category brought into the OECD HPV Chemicals Programme?
     by ICCA-Initiative

7. Review Process Prior to the SIAM:
   - last literature search (update):
     20 January 2003 (Human Health): databases medline, toxline; search profile CAS-No. and special search terms 17 December 2002 (Ecotoxicology): databases CA, biosis; search profile CAS-No. and special search terms

8. Quality check process:
   - As basis for the SIDS-Report the IUCLID was used. All data have been checked and validated by BUA.

9. Date of Submission:
   - 18 February 2003

10. Date of last Update:
11. Comments:

OECD/ICCA - The BUA* Peer Review Process

Qualified BUA personnel (toxicologists, ecotoxicologists) perform a quality control on the full SIDS dossier submitted by industry. This quality control process follows internal BUA guidelines/instructions for the OECD/ICCA peer review process and includes:

- a full (or update) literature search to verify completeness of data provided by industry in the IUCLID/HEDSET
- Review of data and assessment of the quality of data
- Review of data evaluation
- Check of adequacy of selection process for key studies for OECD endpoints, and, where relevant, for non-OECD endpoints by checking original reports/publications
- Review of key study description according robust summaries requirements; completeness and correctness is checked against original reports/publications (if original reports are missing: reliability (4), i.e. reliability not assignable)
- Review of validity of structure-activity relationships
- Review of full SIDS dossier (including SIAR, SIAP and proposal for conclusion and recommendation for further work)

In case of data gaps, review of testing plan or rationale for not testing.

* BUA (GDCh-Beratergremium für Altstoffe): Advisory Committee on Existing Chemicals of the Association of German Chemists (GDCh)
### SIDS INITIAL ASSESSMENT PROFILE

<table>
<thead>
<tr>
<th>CAS No.</th>
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<tr>
<td>Chemical Name</td>
<td>Triethyl phosphite</td>
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<tr>
<td>Structural Formula</td>
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### SUMMARY CONCLUSIONS OF THE SIAR

#### Human Health

No experimental data are available regarding the toxicokinetic behavior and metabolism of triethyl phosphite.

The acute toxicity after oral, dermal, and inhalation exposure is relatively low. The oral LD50s in rats ranged between 1840 mg/kg bw (females) and 2470 mg/kg bw (males). Symptoms of rapid breathing and tremors were observed prior to death. In mice LD50 values above 3700 mg/kg bw were recorded. The 6-hour inhalation LC50 with an aerosol of 1.6-3.5 µm MMAD in rats was between 11,100 mg/m³ (females) and 11,600 mg/m³ (males). Clinical signs included eye and upper respiratory irritation, salivation and rapid, shallow breathing. The dermal LD50 in rabbits was between 2800 mg/kg bw (males) and > 3000 mg/kg bw (females).

Neat triethyl phosphite was slightly irritating to the skin and the eyes of rabbits (OECD TG 404, 405). It was sensitizing to the skin of guinea pigs (OECD TG 406).

The NOAEL in rats was 150 mg/kg bw/day in a 4-week gavage study. At the higher dose (750 mg/kg bw/day), mortality (3 out of 10 animals), a stimulation of the haematopoietic system and inflammatory changes, fibrosis and hyperplasia of the bronchial epithelium in the lungs were found.

Triethyl phosphite was not mutagenic in the Ames test both with and without a metabolic activation system, and including cytotoxic concentrations. In vivo, triethyl phosphite did not induce micronuclei after a single intraperitoneal injection of 1500 mg/kg bw in mice (OECD TG 474).

No data are available regarding the tumorigenic potential of triethyl phosphite.

In a screening study in rats according to OECD TG 421, developmental toxicity was found at dose levels ≥ 320 mg/kg bw/day as evidenced by severely reduced pup survival and reduced pup birth weights (NOAEL: 80 mg/kg bw/day). Effects on fertility were seen in females at 320 mg/kg bw/day in the presence of general toxicity as an increase in time to insemination, severely reduced gestation rate, and an increase in stillbirths and dead pups. Male rats showed changes in the testes at the clearly toxic dose of 640 mg/kg bw/day (NOAEL females: 80 mg/kg bw/day; NOAEL males: 320 mg/kg bw/day).

#### Environment

Triethyl phosphite is a colourless liquid with a melting point of -112 °C, boiling point of 158°C, density of 0.96 g/cm³ and a vapour pressure of 2.6 hPa at 20°C. Due to rapid hydrolysis the determination of water solubility and
log Kow of triethyl phosphite is not appropriate. A log Kow of 0.74 and a water solubility of 15 g/l was calculated. The estimated Henry’s law constant of 2.9 Pa·m³/mol indicates moderate volatility from aqueous solution.

The main degradation process in water is hydrolysis. In acid solution (pH= 4) triethyl phosphite reacts immediately with water to form diethyl phosphite and ethanol. At pH 7 triethyl phosphite hydrolyses completely within 20 minutes, after 3 hours 89.3% diethyl phosphite and 10.7 % monoethyl phosphite are formed. At pH 9 triethyl phosphite is more stable (t1/2water: ca. 5.1 hours), 70 % of the substance remains unhdyolized after 3 hours. In 2 tests on ready biodegradation triethyl phosphite was degraded by 49 - 69 %. Therefore, it did not reach the criteria for ready biodegradability. However, it can be assumed that triethyl phosphite is inherently biodegradable. From two studies on the ready biodegradation of diethyl phosphite it can be concluded that diethyl phosphite is not readily biodegradable but can also be regarded as inherently biodegradable. From the degradation curve it can be assumed that hydrolysis was the prerequisite for biodegradation. It is expected that in the atmosphere a degradation of triethyl phosphite occurs due to indirect photolysis (t 1/2air: ca. 6.6 hours). As the substance hydrolyses under environmental conditions the calculation of a Mackay distribution model is also not appropriate. Due to rapid hydrolysis bioaccumulation of triethyl phosphite is not expected. The calculated log Kow value for diethyl phosphite (log Kow = -0.2) indicates no bioaccumulation potential of the hydrolysis product.

Concerning the toxicity of triethyl phosphite towards aquatic species, reliable experimental results of short term tests with fish, daphnia, and algae are available. The following concentrations are given for triethyl phosphite and are estimations based on the reported results for diethyl phosphite. The acute toxicity determined for fish (Brachydanio rerio) was 251.66 mg/l (96 h LC50) and for daphnia (Daphnia magna) 94.1 mg/l (24 h-EC50). In the growth inhibition test (72 h) with algae (Scenedesmus subspicatus) an EC50 > 73.6 mg/l was determined for both growth rate and biomass.

From the lowest effect value available a PNECaqua of 73.6 µg/l was derived applying an assessment factor of 1000 according to the EU Technical Guidance Document. This factor is justified as short-term effect values from each of the three trophic levels are available.

Tests on terrestrial species are not available.

Exposure

In Europe there is only one producer of triethyl phosphite with a production volume between 1000 and 5000 t/a. The world wide production volume is estimated as 10,000 to 20,000 t/a. Triethyl phosphite is exclusively used as an intermediate for the production of flame retardants, optical brighteners, pesticides, antioxidants, and pharmaceuticals. At production sites effective control techniques are used to minimize exposure of workers. No direct use is known, and no consumer products containing triethyl phosphite were located in the Sponsor country. Triethyl phosphite is not listed in European product registers.

Methyl and ethyl esters of phosphorous acid can be converted by chemical synthesis to nerve gases. Therefore, the production and export of triethyl phosphite is stringently controlled under the International Chemical Weapons Convention.

RECOMMENDATION

The chemical is currently of low priority for further work.
RATIONALE FOR THE RECOMMENDATION AND
NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical possesses properties indicating a hazard for human health. Based on data presented by the Sponsor country, exposure is well controlled in occupational settings and is negligible for consumers. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

Environment: Triethyl phosphite possesses properties indicating a hazard for the environment. Based on data presented by the Sponsor country, exposure to the environment is anticipated to be low, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.
SIDES Initial Assessment Report

1 IDENTIFY

1.1 Identification of the Substance

CAS Number: 122-52-1
IUPAC Name: Triethyl phosphite
Molecular Formula: C₆H₁₅O₃P₁
Structural Formula:

Molecular Weight: 166.16
Synonyms: Phosphorous acid triethyl ester

1.2 Physico-Chemical properties

Triethyl phosphite is a colourless liquid of foul smelling odour with a melting point of –112 °C and boiling point of 158 °C. With a density of 0.96 g/cm³ triethyl phosphite is less heavy than water (Römpp, 1999). The measured vapour pressure at 20°C is 2.6 hPa (Bayer AG, 1989a). A water solubility and log Kow value cannot be determined experimentally due to rapid reaction with water. With KOWWIN 1.66 a log Kow of 0.74 was calculated. Based on this value EPIWIN estimated a water solubility of about 15 g/l. The purity of the substance is 99.3 % (Bayer AG, 2001). Impurities are diethyl phosphonate (< 0.5 % w/w) and triethyl phosphate (< 0.5 % w/w).

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

In the year 2003 in Europe Bayer AG is the only producer of triethyl phosphite with a production volume between 1000 and 5000 t/a. About seven producers of triethyl phosphite are assumed to be located in Asia (India and China). The world-wide production volume is estimated as 10 000 – 20 000 t/a. Further processors of triethyl phosphite amount to about 25 in Europe and are assumed to about 50 worldwide including the USA (Bayer AG, 2002a).

Triethyl phosphite is produced in a closed system by reaction of phosphorous trichlorid and ethanol in the presence of an inorganic or organic base. The product is purified by distillation (Bayer AG, 2002a).

Triethyl phosphite is exclusively used as an intermediate for the manufacturing of different products: flame retardants (about 60 %), optical brighteners (about 15 %), pesticides (about 15 %), antioxidants (about 5 %), and pharmaceuticals (about 5 %).

No direct use is known (Bayer AG, 2002a).
In Denmark, Sweden, Switzerland and Norway triethyl phosphite is not listed in product registers (Danish Product Register, 2002; Swedish Product Register, 2002; Swiss Product Register, 2002; Norwegian Product Register, 2003).

Methyl and ethyl esters of phosphorous acid can be converted by chemical synthesis to nerve gases. Therefore the production and export of triethyl phosphite is stringently controlled under the International Chemical Weapons Convention (1993, CWC Schedules 3B (high volume, dual-use precursor)).

There is no monitoring for triethyl phosphite at the industrial sewage treatment plant outlet at the production site due to the rapid hydrolysis of triethyl phosphite. Due to the water free production process (see above) significant releases of triethyl phosphite and its hydrolysis products can be excluded.

The exhaust from production of triethyl phosphite is connected to a thermal exhaust purification plant. There is no significant emission of triethyl phosphite into the atmosphere.

The residues from production are burnt in a special incineration plant. Therefore there are no emissions of the substance into the terrestrial compartment from production (Bayer AG, 2002a).

There is no information available about environmental releases of triethyl phosphite and its degradation products at other production sites and during processing. However, due to the hydrolysis properties of the substance it may be assumed that also the use of triethylphosphite as chemical intermediate is a water free process.

### 2.2 Environmental Exposure and Fate

The results of the stability experiments carried out by Bayer AG (2001) show that triethyl phosphite hydrolyses rapidly in water. From the guideline study according to the directive 92/69/EEC method C.7 observed with phosphorous-NMR, the following results were obtained in buffered water at 23 °C after 3 hours:

<table>
<thead>
<tr>
<th>pH</th>
<th>Triethyl phosphite</th>
<th>Diethyl phosphite</th>
<th>Monoethyl phosphite</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>0 %</td>
<td>100 %</td>
<td>0 %</td>
</tr>
<tr>
<td>7</td>
<td>0 %</td>
<td>89.34 %</td>
<td>10.66 %</td>
</tr>
<tr>
<td>9</td>
<td>69.88 %</td>
<td>2.35 %</td>
<td>27.77 %</td>
</tr>
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</table>

At pH 4 triethyl phosphite degrades immediately to diethyl phosphite. At pH 7 triethyl phosphite hydrolyses completely within 20 minutes, after 3 hours 89.3 % diethyl phosphite and 10.7 % monoethyl phosphite was formed. At pH 9 triethyl phosphite degrades more slowly ($t_{1/2\text{water}} = 5.1$ hours), after 3 hours 27.77 % monoethyl phosphite and 2.35 % diethyl phosphite were found, 69.88 % of the applied dose were recovered as triethyl phosphite. After 19 h at pH 9 the main degradation product was monoethyl phosphite (93.4 %) (Bayer AG, 2001).

In a preliminary screening test on stability of tri- and diethyl phosphite in water without control of pH the rapid hydrolysis of triethyl phosphite was confirmed. In the same study diethyl phosphite remains stable in pure water over a 95 hours period (86 % recovery after 95 hours) (Bayer AG, 1993).

Thus it can be concluded that the hydrolysis of triethyl phosphite is faster in acidic solutions. The primary degradation products at each pH value are diethyl phosphite and ethanol. The further degradation to monoethyl phosphite was analytically proven at pH-values 7 and 9 but not at pH 4.
Reaction from diethyl phosphite to monoethyl phosphite at pH 9 is rapid whereas at pH 7 it happens more slowly. The hydrolysis product diethyl phosphite seems to be more stable at lower pH values (Bayer AG 2001). According to a preliminary screening test with high amounts of diethyl phosphite in unbuffered water degradation to monoethyl phosphite also occurs at acidic pH after a long period of time (> 100 h) (Bayer AG, 1993).

From the estimated water solubility of 15 g/l and the measured vapor pressure of 2.6 hPa, a Henry’s law constant of 2.9 Pa*m³/mol can be calculated, indicating a moderate volatility of triethyl phosphite from aqueous solutions. The volatility of the main degradation product under neutral conditions, diethyl phosphite, is slightly lower based on the Henry’s law constant of about 1.8 Pa*m³/mol estimated based on a water solubility of 115 g/l and a vapor pressure of 14.9 hPa (data taken from EPIWIN).

Due to hydrolysis the determination of the environmental distribution according the Mackay Fugacity Model Level I is not applicable for triethyl phosphite. For the main degradation product under environmental pH conditions, diethyl phosphite, the target compartments according to a Mackay level 1 fugacity model are water (61.7 %) and air (38.2 %).

Biodegradation was investigated in two ready test systems. In a test according to OECD 301 E guideline 69 % of the initial test concentration was biodegraded after 28 days. The degradation rate is faster at the beginning of the test (ca. 50 % degradation after 7 days) (Bayer AG, 1993).

A closed bottle test in accordance with the method OECD 301 D was conducted with triethyl phosphite as the only source of organic carbon. After 28 days 49 % was degraded by activated sludge with predominantly domestic origin (Bayer AG, 1993).

Based on the available experimental data the degradation rate of triethyl phosphite is 49 - 69 %, but did not reach the criteria for the classification "readily biodegradable".

It could be assumed that triethyl phosphite is inherently biodegradable.

Two studies on the ready biodegradation of diethyl phosphite are available. In a test according to OECD 301C a biodegradation of 8 % was found after 28 days (Bayer AG, 1989). In a second test that was performed according to OECD 301E a biodegradation of 76 % after 27 days was obtained for diethyl phosphite (Bayer AG, 1991). However, the 10d window criterion was not fulfilled. From the degradation curve it can be assumed that the hydrolysis of diethyl phosphite to monoethyl phosphite and ethanol and the further hydrolysis of monoethyl phosphite to ethanol and phosphorous acid was the prerequisite for biodegradation. Summarising, the hydrolysis product diethyl phosphite cannot be regarded as readily but inherently biodegradable.

Direct photolysis of triethyl phosphite is not expected because the substance does not absorb light at wavelengths > 290 nm.

Triethyl phosphite entering into the atmosphere is expected to be photodegraded rapidly by OH-radicals. The calculated half-life of triethyl phosphite in air due to indirect photodegradation is t½air = 6.6 hours (0.5E+6 OH radicals/cm3) (Bayer AG, 2002b).

Bioconcentration factors (BCF) cannot be measured due to hydrolysis. Determination of the octanol-water partition coefficient for triethyl phosphite is not appropriate for the same reason. The calculated log KOW values for triethyl phosphite (log KOW = 0.74) and the degradation product diethyl phosphite (log KOW = -0.2) indicates that there is no potential for bioaccumulation in aquatic organisms (Bayer AG, 2002b).
2.3  Human Exposure

Triethyl phosphite is exclusively used as an intermediate for chemical synthesis. No direct use is known.

2.3.1  Occupational Exposure

During manufacture and processing of triethyl phosphite workers may be exposed, with the dermal and inhalation routes being the primary routes of exposure.

In Germany, there is no workplace limit concentration laid down for triethyl phosphite.

At Bayer AG, triethyl phosphite is produced in a closed system.

The homologue trimethyl phosphite has an odor threshold of 0.00010 pm (Amoore and Hautala, 1983), and triethyl phosphite is assumed to have a very low odor threshold, too. Therefore, any leakage would probably be recognized due to the strong foul-smelling odor of triethyl phosphite.

Workplace measurements of triethyl phosphite were not performed.

Investigations of the workplace where triethyl phosphite is produced have been performed according to German Technical Guidance TRGS 402. This includes regular surveys in the working area for any possible exposure to a dangerous substance at different work situations and appropriate control measures.

To protect workers several precautionary and protective measures are taken. These measures include technical equipment like suction devices at filling and sampling stations as well as appropriate personal protection equipment as prescribed in detail for different work situations e.g. during sampling, maintenance, and repair work. During sampling, for instance, gas filter masks, goggles, and gloves have to be worn. Depending on the work to be done during maintenance, gas filter masks or a respirator with independent air supply have to be used as well as full protective clothing. Downstream users of triethyl phosphite are informed by way of a material safety data sheet on the recommended safety measures, including personal protective equipment (such as goggles, face shields, gloves, aprons, personal respirators), and local and/or general ventilation systems. No exposure measurements were available for workers involved in down-stream uses of triethyl phosphite.

On-site, triethyl phosphite is transported in pipelines. To customers triethyl phosphite is mainly transported in ISO tank containers, and only minor quantities are transported in metal drums.

2.3.2  Consumer Exposure

Exposure of the general public:

The only known use of triethyl phosphite is that as an industrial intermediate. Due to the high reactivity of the chemical, triethyl phosphite is not expected to be present above trace amounts in end-products (such as flame retardants, optical brighteners, pesticides, antioxidants, and pharmaceuticals), and hence exposure of consumers to triethyl phosphite through these products is not considered relevant (Bayer AG, 2002a).

With respect to the rapid hydrolysis indirect exposure via the environment is not expected.
3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

No experimental data are available regarding toxicokinetic behavior and metabolism of triethyl phosphite.

3.1.2 Acute Toxicity

Inhalation

An acute inhalation study was done with male and female Fisher 344 rats. After an exposure period of 6 hours the calculated LC$_{50}$ was 11.6 mg/l for males and 11.1 mg/l for females with an aerosol of 1.6 - 3.5 µm MMAD. A similar study in CD-1 mice gave LC$_{50}$ values of 6.2 and 9.2 mg/l for male and female animals, respectively. In both species, signs of toxic stress included eye and upper respiratory irritation, salivation and rapid, shallow breathing; most deaths occurred within 24 hours following treatment. No quantitative data regarding the dose-response curve were reported in the study (Kinkead et al., 1992).

The available study is considered plausible and valid as it meets the main requirements for assessing and reporting acute inhalation toxicity results.

Conclusion: The acute inhalation toxicity is low. The 6-hour LC$_{50}$ in rats was between 11 100 mg/m$^3$ (females) and 11 600 mg/m$^3$ (males). Clinical signs included eye and upper respiratory irritation, salivation and rapid, shallow breathing.

Dermal

In rabbits, the 24h occlusive application of 2000 to 3000 mg/kg bw triethyl phosphite on 30 % of body surface led to an LD$_{50}$ of 2800 mg/kg bw in males and an LD$_{50}$ of > 3000 mg/kg bw in females (Kinkead et al., 1992). Clinical signs of toxicity were not reported.

Conclusion: The acute dermal toxicity is low. The LD$_{50}$ in rabbits was between 2800 mg/kg bw (males) and > 3000 mg/kg bw (females).

Oral

An early study showed an LD$_{50}$ of > 2.5 ml/kg bw (2385 mg/kg bw) in male rats. No clinical symptoms were observed at the highest dose level of 2.5 ml/kg bw (Bayer AG, 1959).

In a study with male and female Fisher 344 rats triethyl phosphite was administered in doses from 1000 to 4000 mg/kg bw. The calculated LD$_{50}$ was 2470 mg/kg bw for males and 1840 mg/kg bw for females. Symptoms of rapid breathing and tremors were observed prior to death (Kinkead et al., 1992).

In mice the toxicity of triethyl phosphite after oral administration was determined by Kinkead et al. (1992). The dose range was from 2000 to 5000 mg/kg bw and the LD$_{50}$ was determined as 3720 mg/kg bw for males and 3800 mg/kg bw for females.

No quantitative data regarding dose-response curves were reported in any study.
Conclusion: The acute oral toxicity is relatively low. The LD₅₀s in rats ranged between 1840 mg/kg bw (females) and 2470 mg/kg bw (males). Symptoms of rapid breathing and tremors were observed prior to death. In mice LD₅₀ values above 3700 mg/kg bw were recorded.

3.1.3 Irritation

Skin Irritation

A study according to OECD guideline 404 (1980) employing 6 albino-rabbits revealed slightly irritating effects on the skin after 4 hours of semi-occlusive exposure to the undiluted test substance. All animals showed slight or clearly visible erythema at the treated sites up to 48 hours after exposure. At day 7, slight erythema (grade 1) still persisted in 5 animals, but had resolved in all but one animal at day 10. None of the animals showed edema at any of the observations. (Suberg, 1983). Further data confirm this result (Kinkead et al., 1992).

Conclusion: Neat triethyl phosphite was slightly irritating to the skin of rabbits (OECD 404).

Eye Irritation

A study according to OECD guideline 405 was performed and showed slightly irritating effects on the eyes of 3 male rabbits. All animals showed slight or clearly visible conjunctival erythema in the treated eyes (grade 1 or 2). Slight chemonosis and increased secretion were recorded in two animals, each. The findings appeared within one hour and were completely reversible within 48 hours (Suberg, 1983). Another study employing 9 rabbits (6 eyes unwashed and 3 washed) showed moderate but quickly reversible irritating effects on the eyes. Effects were more severe after washing with water (Kinkead et al., 1992).

Conclusion: Triethyl phosphite was slightly irritating to the eyes of rabbits (OECD 405).

3.1.4 Sensitisation

A study according to OECD guideline 406 and performed under GLP conditions showed sensitizing effects in 19 out of 20 animals treated with triethyl phosphite (purity 98.8 %) in the guinea pig maximization test (Dreist and Kolb, 1993).

Conclusion: Triethyl phosphite was sensitizing to the skin in guinea pigs.

3.1.5 Repeated Dose Toxicity

A study according to OECD guideline 407 (1981) was performed under GLP conditions with repeated oral dosing by gavage to rats (32 days treatment) at doses of 0, 30, 150, and 750 mg/kg bw/day. At the highest exposure level, an increase in mortality in both sexes and, in males only, changes in blood parameters indicative of a stimulation in erythropoiesis were found (increases in red blood cell count, hemoglobin, hematocrit together with a decrease in mean corpuscular volume and mean cell volume) together with increases in various organ weights, in particular of lungs and adrenals. Body weight gain, and food and water consumption were markedly reduced when compared to the controls. Histopathological examination of high dose animals revealed effects in the lung, such as inflammatory changes, fibrosis and hyperplasia of bronchial epithelium. The study did not include the histopathological examination of spinal cord, stomach, small and large intestines, thymus, thyroid, trachea, gonads, accessory sex organs, urinary bladder, lymph nodes, peripheral nerve, bone marrow. A NOAEL of 150 mg/kg bw/day was established (Schladt and Hartmann, 1992).
Conclusion: The NOAEL in rats was 150 mg/kg bw/day in a 4-week study. At the higher dose (750 mg/kg bw/day) mortality (3 out of 10 animals), a stimulation of the haematopoietic system and inflammatory changes, fibrosis and hyperplasia of the bronchial epithelium in the lungs were found.

3.1.6 Mutagenicity

Studies in Animals

In vitro Studies

There was no indication of a potential to induce gene mutations in the Ames test with four different strains of *Salmonella typhimurium* (TA98, TA100, TA 1535, TA1537) both with and without metabolic activation by rat liver S9 mix. The test was performed including cytotoxic concentrations (Herbold, 1988).

Conclusion: Triethyl phosphite was not mutagenic in the Ames test both with and without a metabolic activation system, and including cytotoxic concentrations.

In vivo Studies

One study is available regarding chromosomal damage in-vivo. The in-vivo micronucleus assay was conducted according to OECD guideline 474 and under GLP conditions in male and female NMRI mice dosed with 1500 mg/kg bw by single intraperitoneal injection. Triethyl phosphite treated groups were sacrificed at 16 hours, 24 hours or 48 hours after treatment. There were relevant toxic effects on the bone marrow as evidenced by a clear change in the ratio of polychromatic to normochromatic erythrocytes at 16 hours after treatment, but there were no indication of a clastogenic activity. In none of the triethyl phosphite treated groups were micronuclei induced. The following symptoms were recorded for up to 48 hours after a single intraperitoneal injection of 1500 mg/kg bw in a pre-test: apathy, roughened fur, staggering gait, sternal and lateral recumbency, spasm, shivering and difficulty in breathing (Herbold, 1992).

Conclusion: In vivo, triethyl phosphite did not induce micronuclei after a single intraperitoneal injection of 1500 mg/kg bw in mice. The study was compliant to OECD TG 474.

3.1.7 Carcinogenicity

No data are available regarding the tumorigenic potential of triethyl phosphite.

3.1.8 Toxicity for Reproduction

In a screening study according to OECD TG 421 effects of triethyl phosphite on fertility and fetal development were examined. Doses of 0, 10, 80, 320 and 640 mg/kg bw/day were used for oral administration (gavage) to rats. Groups of 12 male and female Wistar rats each were treated (control group: 15 males and 15 females). F0-Animals were treated from 2 weeks before mating to the end of gestation and up to 6 days of lactation. Males were killed after 36 to 37 days of treatment. Females and pups were killed on days 4 to 6 post partum. Ovaries, mammae, testes, epididymides and macroscopically altered tissues of F0 animals were examined histologically. Parameters of general toxicity and fertility, as well as pre- and post-natal development were recorded.

General toxicity: Animals of both sexes in the high dose group (640 mg/kg bw/day) exhibited clear clinical signs of systemic toxicity (e.g. piloerection, sunken sides, tremors, salivation immediately after dosing, recumbency) and body weight loss (> 14 % decrease relative to controls in males and females). All females of this group were killed in moribund condition. Similar signs of toxicity were seen in individual females of the 320 mg/kg bw/day group. Slight weight loss was recorded in
individual females after exposure to 80 mg/kg bw/day before the increase of weight due to gestation. Salivation was observed in males of all dose groups with a dose-related increase and in females of the 80, 320 and 640 mg/kg bw/day groups.

Effects on Fertility

Fertility: Histopathology showed minimal to slight degeneration in the germinal epithelium of testes, and apoptosis and/or regenerative hyperplasia in the testes and epididymides, after exposure to the clearly paternally toxic dose level of 640 mg/kg bw/day. Relative testes weights (%) were 0.87, 0.89, 0.91, 0.85, and 0.98 (statistically significant) for controls, 10, 80, 320 and 640 mg/kg bw/day groups, respectively. There was no significant difference in absolute testes weights between the groups. In females, histopathology revealed slight proliferation / secretion in the mammary gland together with mucification in the cervix and vagina in all females at 640 mg/kg bw/day, which were sacrificed in moribund state either after 8 to 10 days of pairing or during early gestation. No histopathological changes were recorded in reproductive organs up to and including a dose of 320 mg/kg bw/day.

Only 5 of 12 females were inseminated in the 640 mg/kg bw/day group. Evaluation of other data regarding reproductive performance, including early postnatal development of pups for the 640 mg/kg bw/day group was not possible.

At a dose level of 320 mg/kg bw/day an increase in time to insemination, slightly decreased duration of gestation, a severely reduced gestation rate, distinctly increased number of stillborn/dead F1 pups, and a distinctly decreased number of viable/total number of pups were recorded. Pups showed severely reduced birth weights, hypothermia and severely reduced survival.

No effects on the other reproductive parameters (insemination index, fertility index, numbers of corpora lutea and implantation sites, prenatal loss, litter size) were detected up to and including a dose level of 320 mg/kg bw/day.

Developmental Toxicity

Fetal development: In F1, the sex ratio, mortality and weights were not affected by treatment up to and including doses of 80 mg/kg bw/day, while evaluation was not possible at higher doses as there were no surviving pups. No externally malformed pups were observed. (Bayer AG, 2002c).

Conclusion

In a screening study in rats according to OECD TG 421, developmental toxicity was found at dose levels ≥ 320 mg/kg bw/day as evidenced by severely reduced survival and reduced pup birth weights (NOAEL: 80 mg/kg bw/day).

Effects on fertility were seen in females at 320 mg/kg bw/day in the presence of general toxicity as an increase in time to insemination, severely reduced gestation rate, and an increase in stillbirths and dead pups. Male rats showed changes in the testes at the severely toxic dose of 640 mg/kg bw/day.

(NOAEL females: 80 mg/kg bw/day; NOAEL males: 320 mg/kg bw/day).

3.1.9 Experience with human exposure

No data are available regarding experience with human exposure to triethyl phosphite.
3.2 Initial Assessment for Human Health

No experimental data are available regarding the toxicokinetic behavior and metabolism of triethyl phosphite.

The acute toxicity after oral, dermal, and inhalation exposure is relatively low. The oral LD$_{50}$s in rats ranged between 1840 mg/kg bw (females) and 2470 mg/kg bw (males). Symptoms of rapid breathing and tremors were observed prior to death. In mice LD$_{50}$ values above 3700 mg/kg bw were recorded. The 6-hour inhalation LC$_{50}$ with an aerosol of 1.6 - 3.5 µm MMAD in rats was between 11 100 mg/m$^3$ (females) and 11 600 mg/m$^3$ (males). Clinical signs included eye and upper respiratory irritation, salivation and rapid, shallow breathing. The dermal LD$_{50}$ in rabbits was between 2800 mg/kg bw (males) and > 3000 mg/kg bw (females).

Neat triethyl phosphite was slightly irritating to the skin and the eyes of rabbits (OECD TG 404 and 405). It was sensitizing to the skin of guinea pigs (OECD TG 406).

The NOAEL in rats was 150 mg/kg bw/day in a 4-week gavage study. At the higher dose (750 mg/kg bw/day) mortality (3 out of 10 animals), a stimulation of the haematopoietic system and inflammatory changes, fibrosis and hyperplasia of the bronchial epithelium in the lungs were found.

Triethyl phosphite was not mutagenic in the Ames test both with and without a metabolic activation system, and including cytotoxic concentrations. In vivo, triethyl phosphite did not induce micronuclei after a single intraperitoneal injection of 1500 mg/kg bw in mice (OECD TG 474).

No data are available regarding the tumorigenic potential of triethyl phosphite.

In a screening study in rats according to OECD TG 421, developmental toxicity was found at dose levels $\geq$ 320 mg/kg bw/day as evidenced by severely reduced pup survival and reduced pup birth weights (NOAEL: 80 mg/kg bw/day). Effects on fertility were seen in females at 320 mg/kg bw/day in the presence of general toxicity as an increase in time to insemination, severely reduced gestation rate, and an increase in stillbirths and dead pups. Male rats showed changes in the testes at the severely toxic dose of 640 mg/kg bw/day (NOAEL females: 80 mg/kg bw/day; NOAEL males: 320 mg/kg bw/day).

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Concerning the aquatic effects short term toxicity tests are available for each trophic level. The studies were performed in accordance with the principles of Good Laboratory Practice (GLP).

Triethyl phosphite reacts rapidly with water forming di- and monoethyl phosphite depending on pH. Therefore the toxicity of triethyl phosphite itself cannot be tested properly. Tests with the hydrolysis product diethyl phosphite at pH 7 are available. For the hydrolysis product at pH 9 monoethyl phosphite no tests were conducted.

Acute Toxicity Test Results

Acute toxicity to fish (*Brachydanio rerio*) has been tested in a static system according to the method C.1 of the directive 67/548/EEC. From the hydrolysis study described in section 2.1 it is known that triethyl phosphite hydrolyses completely within 20 min at pH 7. A preliminary test showed that the degradation product diethyl phosphite remains stable (> 80% recovery) for 96 h (duration of the fish test). For this reason the test was started 2 hours after inserting triethyl phosphite into the test solution in order to ensure complete hydrolysation. The degradation product, diethyl phosphite was
followed with GC-analysis in place of triethyl phosphite during the study. The GC-analysis showed that the measured concentrations of diethyl phosphite at test start were about 60% of the concentration that could be calculated from the triethyl phosphite concentration assuming full hydrolysis. Within the first 24 h the concentrations further decreased and remained then nearly constant throughout the test. As the measured diethyl phosphite concentrations were lower than the calculated nominal values, the test results are based on measured diethyl phosphite concentrations. After 96 hours an effective LC$_{50}$ concentration of 209.1 mg/l was obtained for diethyl phosphite that corresponds to an effective estimated concentration of 251.6 mg/l triethyl phosphite (Bayer AG 1993). As only the diethyl phosphite was analytically measured, it cannot be excluded that the toxicity observed in the study was also influenced by the presence of further hydrolysis products or the parent compound.

With *Daphnia magna* an acute test was performed according to the guideline proposal of the German Federal Environmental Agency without analytical monitoring. The toxicity to *Daphnia magna* was tested with diethyl phosphite during 24 h resulting in an EC$_{50}$ of 78.2 mg/l (nominal concentration). The stability of diethyl phosphite over a 24 hours period was demonstrated in the above mentioned preliminary test before testing acute toxicity to fish. As in this study diethyl phosphite itself was used instead of triethyl phosphite, and therefore influence of incomplete hydrolysis on the test concentrations is excluded, it can be assumed that the concentrations remain stable during the duration of the test. The reported result corresponds to a calculated nominal EC$_{50}$ value of 94.1 mg/l triethyl phosphite (Bayer AG 1989b). It can be discussed that with the direct use of diethyl phosphite as test substance the estimation of the toxicity of the parent compound including all hydrolysis products is arguable. However, the uncertainty behind this approach is regarded to be acceptable as diethyl phosphite is the main degradation product under environmental pH conditions.

For the performance of the growth inhibition test for algae, the results of the preliminary test before testing fish toxicity (see above) were taken into account. Triethyl phosphite hydrolyses completely within 20 min at pH 7 and the degradation product diethyl phosphite remains stable for 72 h (duration of algae test.) Therefore it was proceeded as in the fish toxicity test mentioned before. In order to ensure that hydrolysis of triethyl phosphite to diethyl phosphite was complete, the test was started 2 hours after inserting triethyl phosphite. The test substance concentrations were determined by TOC measurement and were found to remain nearly constant within the 72 h exposure time. With the green algae *Scenedesmus subspicatus* a 72 h-EC$_{50}$ value greater than 73.6 mg/l (effective concentration related to triethyl phosphite) was determined for both growth rate and biomass. The 72 h-NOEC-value of triethyl phosphite is about 37 mg/l (Bayer AG 1999).

**Toxicity to Microorganisms**

Regarding the toxicity to microorganisms, an O$_2$-consumption test in accordance with the ISO Norm 8192 with activated sludge during 3 hours was performed with triethyl phosphite and a nominal EC$_{50}$ of 4720 mg/l was determined (Bayer AG 1993).

Since short-term tests for each of the three trophic levels are available, an assessment factor of 1000 was applied for the derivation of the PNECaqua according to EU Technical Guidance Document. From the lowest effect value available, the PNECaqua is calculated to be 73.6 µg/l.

### 4.2 Terrestrial Effects

No data available.
4.3 Other Environmental Effects

No data available.

4.4 Initial Assessment for the Environment

When triethyl phosphite is released into the environment, in the hydrosphere it hydrolyses at pH 4 and 7 rapidly to diethyl phosphite in less than 3 hours. In basic buffered water (pH 9) the primary hydrolysis occurs slower. In basic buffered water (pH 9) diethyl phosphite hydrolyses further to monoethyl phosphite. At pH 7 this reaction is slower. In unbuffered water diethyl phosphite is stable for a longer period (after 95 hours still 86 % diethyl phosphite).

In air, the substance is indirectly photodegradable with $t_{1/2\text{air}} = 6.6$ hours. Triethyl phosphite and its hydrolysis product diethyl phosphite are not readily biodegradable but can be regarded as inherently biodegradable.

Due to hydrolysis, bioaccumulation is not expected. The calculated log Kow values of 0.74 for triethyl phosphite and of −0.2 for the hydrolysis product diethyl phosphite indicate no bioaccumulation potential.

The effect concentrations for triethyl phosphite estimated from the results for diethyl phosphite of the aquatic tests for fish, daphnia, algae and the results of the bacteria test were as following:

- **Fish**: *Brachydanio rerio* with a 96 h-EC$_{50}$ of 251.6 mg/l
- **Daphnia**: *Daphnia magna* with a 24 h-EC$_{50}$ of 94.1 mg/l
- **Algae**: *Scenedesmus subspicatus* with a 72h-EC$_{50}$ of >73.6 mg/l (growth rate and biomass)
- **Microorganisms**: Activated sludge with a 3h-EC$_{50}$ of 4720 mg/l.

Following the EU Technical Guidance Document, for the derivation of the PNECaqua an assessment factor of 1000 is chosen since at least one short-term EC$_{50}$ or LC$_{50}$ value from each of the three trophic levels is available. Using the lowest effect concentration: *Scenedesmus subspicatus* EC$_{50}$ > 73.6 mg/l, a PNECaqua of > 73.6 µg/l is derived.

5 RECOMMENDATIONS

Environment:

The chemical is currently of low priority for further work. Triethyl phosphite possesses properties indicating a hazard for the environment. Based on data presented by the Sponsor country, exposure to the environment is anticipated to be low, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

Human Health:

The chemical is currently of low priority for further work. Triethyl phosphite possesses properties indicating a hazard for human health. Based on data presented by the Sponsor country, exposure is well controlled in occupational settings and is negligible for consumers. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.
6 REFERENCES


Bayer AG (1989b). Internal study 98A/89: Acute Toxicity Test with *Daphnia magna* to Diethyl phosphite according to the German BUA-Proposal of Mai 1984 (1989.08.10).

Bayer AG (1989c). Internal study 98A/89: Biodegradation of diethyl phosphite according to OECD 301C.

Bayer AG (1991). Internal study 98 A/89 O: Biodegradation of diethyl phosphite according to OECD 301E.


- Toxicity to Bacteria according to ISO 8192,1986
- Acute Toxicity to Fish according to Directive 67/548/EEC,1992 (incl. a preliminary test on stability of Tri- and Diethyl phosphite in water)
- Modified OECD Screening Test according to Directive 84/449/EEC, 1984


Bayer AG (2002a). Triethyl phosphite - internal data on production, processing, use pattern, and workplace exposure; unpublished.

Bayer AG (2002b). Calculation of

- Log Octanol-Water Partition Coefficient with SRC-KOWWIN v.1.66, 2000


Herbold BA (1988). Triethyl phosphite – Salmonella/microsome tes to evaluate for point mutagenic effects; unpublished report of Bayer AG, No. 17112, September 6, 1988


Norwegian Product Register (2003). Communication to the OECD.


Swedish Product Register (2002). Communication to the OECD.

Swiss Product Register (2002). Communication to BUA.

# IUCLID Data Set

**Existing Chemical**
- ID: 122-52-1
- CAS No.: 122-52-1
- EINECS Name: triethyl phosphate
- EC No.: 204-552-5
- TSCA Name: Phosphorous acid, triethyl ester
- Molecular Formula: C6H15O3P

**Producer related part**
- Company: Bayer AG
- Creation date: 18.08.1993

**Substance related part**
- Company: Bayer AG
- Creation date: 18.08.1993
- Status: 
- Memo: X AKTUELL EG / ICCA

**Printing date**: 12.01.2005  
**Revision date**: 27.05.1994  
**Date of last update**: 12.01.2005  
**Number of pages**: 43

**Chapter (profile)**: Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10  
**Reliability (profile)**: Reliability: without reliability, 1, 2, 3, 4  
**Flags (profile)**: Flags: without flag, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS
# OECD SIDS TRIETHYL PHOSPHITE

## 1. GENERAL INFORMATION

### 1.0.1 APPLICANT AND COMPANY INFORMATION

### 1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

### 1.0.3 IDENTITY OF RECIPIENTS

### 1.0.4 DETAILS ON CATEGORY/TEMPLATE

## 1.1.0 SUBSTANCE IDENTIFICATION

### 1.1.1 GENERAL SUBSTANCE INFORMATION

- **Purity type:**
- **Substance type:** Organic
- **Physical status:** Liquid
- **Purity:**
- **Colour:**
- **Odour:**

**Flag:** Critical study for SIDS endpoint

### 1.1.2 SPECTRA

## 1.2 SYNONYMS AND TRADENAMES

**PHOSPHOROUS ACID, TRIETHYL ESTER**

**Flag:** Critical study for SIDS endpoint

**TRIETHYL PHOSPHITE**

**Flag:** Critical study for SIDS endpoint

**TRIETHYLESTER DER PHOSPHORGEN SÄURE**

**Flag:** Critical study for SIDS endpoint

**TRIETHYLPHOSPHIT**

**Flag:** Critical study for SIDS endpoint
1.3 IMPURITIES

- **Purity:**
  - **CAS-No:** 762-04-9
  - **EC-No:** 212-091-6
  - **EINECS-Name:** diethyl phosphonate
  - **Molecular formula:**
  - **Value:** < .5 % w/w

- **Flag:** Critical study for SIDS endpoint

- **Purity:**
  - **CAS-No:** 78-40-0
  - **EC-No:** 201-114-5
  - **EINECS-Name:** triethyl phosphate
  - **Molecular formula:**
  - **Value:** < .5 % w/w

- **Flag:** Critical study for SIDS endpoint

1.4 ADDITIVES

1.5 TOTAL QUANTITY

- **Quantity:** - tonnes in 2002

- **Remark:** Production volume in Europe: 1,000-5,000 tonnes/a
  Estimated world-wide production volume: 10,000-20,000 tonnes/a

- **Flag:** Critical study for SIDS endpoint

1.6.1 LABELLING

- **Labelling:** provisionally by manufacturer/importer
- **Specific limits:**
- **Symbols:** Xi, , ,
- **Nota:**
- **R-Phrases:** (10) Flammable
  (43) May cause sensitization by skin contact
  (52/53) Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment

- **S-Phrases:** (24) Avoid contact with skin

- **Flag:** Critical study for SIDS endpoint
1.6.2 CLASSIFICATION

Classified : provisionally by manufacturer/importer
Class of danger : Irritating
R-Phrases : (10) Flammable
            (43) May cause sensitization by skin contact
Specific limits :  

Flag : Critical study for SIDS endpoint

09.03.2000

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : type
Category : Use in closed system

Flag 22.12.2004 : Critical study for SIDS endpoint

Type of use : industrial
Category : Chemical industry: used in synthesis

Flag 22.12.2004 : Critical study for SIDS endpoint

Type of use : use
Category : Intermediates

Flag 22.12.2004 : Critical study for SIDS endpoint

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE
1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Remark: no occupational exposure limit values
Flag: Critical study for SIDS endpoint
23.11.2000

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

Classified by: other: VwVwS (Anhang 3)
Labelled by:
Class of danger: 1 (weakly water polluting)
17.05.2000

1.8.4 MAJOR ACCIDENT HAZARDS

Legislation: Stoerfallverordnung (DE)
Substance listed: no
No. in Seveso directive:

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS
1.12 LAST LITERATURE SEARCH

**Type of search**  :  Internal and External  
**Chapters covered**  :  
**Date of search**  :  

**Remark**  :  Toxicology  08/2002  
               Ecotoxicology and Environmental Fate 09/2002  
**Flag**  :  Critical study for SIDS endpoint  
            29.11.2002

1.13 REVIEWS
## 2.1 MELTING POINT

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<tr>
<th>Value</th>
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<td>Reliability</td>
<td>(2) valid with restrictions</td>
</tr>
<tr>
<td>Flag</td>
<td>Data from handbook or collection of data</td>
</tr>
<tr>
<td>Date</td>
<td>24.01.2003</td>
</tr>
</tbody>
</table>

## 2.2 BOILING POINT

<table>
<thead>
<tr>
<th>Value</th>
<th>158 °C at 1013.25 hPa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remark</td>
<td>54°C at 19 hPa</td>
</tr>
<tr>
<td>Reliability</td>
<td>(2) valid with restrictions</td>
</tr>
<tr>
<td>Flag</td>
<td>Critical study for SIDS endpoint</td>
</tr>
<tr>
<td>Date</td>
<td>24.01.2003</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Value</th>
<th>156.4 °C at 1013.25 hPa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decomposition</td>
<td>other: extrapolated from measured values</td>
</tr>
<tr>
<td>Method</td>
<td></td>
</tr>
<tr>
<td>Year</td>
<td></td>
</tr>
<tr>
<td>GLP</td>
<td></td>
</tr>
<tr>
<td>Test substance</td>
<td></td>
</tr>
</tbody>
</table>

| Reliability | (2) valid with restrictions |
| Date        | 24.01.2003 |

<table>
<thead>
<tr>
<th>Value</th>
<th>156 - 158 °C at 1013 hPa</th>
</tr>
</thead>
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<tr>
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</tr>
<tr>
<td>Date</td>
<td>24.01.2003</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Value</th>
<th>157.9 °C at 1013.25 hPa</th>
</tr>
</thead>
<tbody>
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<td>Reliability</td>
<td>(2) valid with restrictions</td>
</tr>
<tr>
<td>Date</td>
<td>24.01.2003</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result</th>
<th>Beilstein's reported boiling point values are in the range of 154-159°C (at 987-1010 hPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reliability</td>
<td>(2) valid with restrictions</td>
</tr>
<tr>
<td>Date</td>
<td>24.01.2003</td>
</tr>
</tbody>
</table>

(1) (2) (3) (4) (5)
## 2.3 DENSITY

<table>
<thead>
<tr>
<th>Type</th>
<th>Value</th>
<th>Reliability</th>
<th>Flag</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>density</td>
<td>(2) valid with restrictions</td>
<td>Critical study for SIDS endpoint</td>
</tr>
<tr>
<td></td>
<td>.96 at °C</td>
<td>Data from handbook or collection of data</td>
<td></td>
</tr>
<tr>
<td></td>
<td>.95 g/cm³ at 20 °C</td>
<td>(4) not assignable secondary literature</td>
<td></td>
</tr>
</tbody>
</table>

Remark: Beilstein's reported density values are in the range of 0.961-0.9687 g/cm³ (4/20°C).

## 2.3.1 GRANULOMETRY

## 2.4 VAPOUR PRESSURE

<table>
<thead>
<tr>
<th>Value</th>
<th>2.6 hPa at 20 °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decomposition</td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td>other (measured): Röck apparatus (dynamic method)</td>
</tr>
<tr>
<td>Year</td>
<td>1989</td>
</tr>
<tr>
<td>GLP</td>
<td>no</td>
</tr>
<tr>
<td>Test substance</td>
<td>other TS: Triethyl phosphite, purity 99.2%</td>
</tr>
</tbody>
</table>

Reliability: (2) valid with restrictions
Study well documented, meets generally scientific principle measurements acceptable for assessment

Flag: Critical study for SIDS endpoint

<table>
<thead>
<tr>
<th>Value</th>
<th>3.2 hPa at 24 °C</th>
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</thead>
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<tr>
<td>Reliability</td>
<td>(2) valid with restrictions</td>
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<tr>
<td>Flag</td>
<td>Critical study for SIDS endpoint</td>
</tr>
<tr>
<td>Test substance</td>
<td>Data from handbook or collection of data</td>
</tr>
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</table>
### 2. PHYSICAL-CHEMICAL DATA

<table>
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<th>Property</th>
<th>Value</th>
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</thead>
<tbody>
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<td>Decomposition</td>
<td>14.9 hPa at °C</td>
</tr>
<tr>
<td>Method</td>
<td>other (calculated): EPIWIN</td>
</tr>
<tr>
<td>Year</td>
<td>2003</td>
</tr>
<tr>
<td>Test substance</td>
<td>other TS: Diethyl phosphite</td>
</tr>
</tbody>
</table>

**Remark**: Diethyl phosphite is a hydrolysis product of triethyl phosphite

**Reliability**: (2) valid with restrictions

**Flag**: Critical study for SIDS endpoint

---

### 2.5 PARTITION COEFFICIENT

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Octanol-water</td>
<td>.74 at °C</td>
</tr>
<tr>
<td>pH value</td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td>other (calculated): with SRC-KOWWIN v.1.66</td>
</tr>
<tr>
<td>Year</td>
<td>2002</td>
</tr>
<tr>
<td>Test substance</td>
<td>as prescribed by 1.1 - 1.4</td>
</tr>
</tbody>
</table>

**Remark**: The calculated log Pow of triethyl phosphite is a QSAR estimation. Triethyl phosphite hydrolyses within 3 hours to diethyl phosphite (see chapter 3.1.2: Stability in Water): log Pow of diethyl phosphite was calculated to -0.2

**Reliability**: (2) valid with restrictions

**Flag**: Critical study for SIDS endpoint

---

### 2.6.1 SOLUBILITY IN DIFFERENT MEDIA

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solubility in</td>
<td>Water</td>
</tr>
<tr>
<td>Water</td>
<td></td>
</tr>
</tbody>
</table>

**Remark**: Experimentally measured by HPLC, standard deviation +- 0.02 (6 measurements). Application of HPLC method is problematic due to hydrolysis of triethyl phosphite.

**Reliability**: (2) valid with restrictions

**Flag**: Critical study for SIDS endpoint
OECD SIDS TRIETHYL PHOSPHITE
2. PHYSICAL-CHEMICAL DATA ID: 122-52-1
DATE: 12.01.2005

pH value : 
concentration : at °C
Temperature effects : 
Examine different pol. : 
pKa : at 25 °C
Description : 
Stable : 
Deg. product : 
Method : other: Calculation with EPIWIN of US EPA
Year : 2003
GLP : 
Test substance :

Remark : Not applicable for triethyl phosphate due to hydrolysis
Result : A water solubility cannot be determined experimentally for triethyl phosphate due to rapid reaction with water. EPIWIN estimated a water solubility of about 15 g/l.
For the degradation product diethyl phosphate, a water solubility of 115 g/l was estimated by EPIWIN.
Reliability : (2) valid with restrictions
Flag : Accepted calculation method
22.12.2004

Solubility in : other: Water and organics
Value : at °C
pH value : 
concentration : at °C
Temperature effects : 
Examine different pol. : 
pKa : at 25 °C
Description : 
Stable : 

Remark : unsoluble in water, miscible with most organic solvents
Reliability : (2) valid with restrictions
Flag : Data from handbook or collection of data
22.12.2004

2.6.2 SURFACE TENSION

Result : 24.26 mN/m at 20°C
24.1 mN/m at 24°C
Reliability : (2) valid with restrictions
Flag : Data from handbook or collection of data
12.01.2005

2.7 FLASH POINT

Value : 52 °C
Type : closed cup
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<th>Method</th>
<th>other: DIN 51755</th>
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<tbody>
<tr>
<td>Year</td>
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<tr>
<td>GLP</td>
<td></td>
</tr>
<tr>
<td>Test substance</td>
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<table>
<thead>
<tr>
<th>Reliability</th>
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<table>
<thead>
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<th>54.4 °C</th>
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<table>
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<tr>
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<th>(2) valid with restrictions Data from handbook or collection of data</th>
</tr>
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<tbody>
<tr>
<td>Flag</td>
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<tr>
<td>24.01.2003</td>
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</table>

**2.8 AUTO FLAMMABILITY**

**2.9 FLAMMABILITY**

<table>
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<tr>
<th>Result</th>
<th>ignition temperature: 250°C</th>
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**2.10 EXPLOSIVE PROPERTIES**

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<table>
<thead>
<tr>
<th>Remark</th>
<th>lower limit: 3.75 vol% upper limit: 42.5 vol% both in air at 1000 Pa</th>
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</thead>
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<td>(4) not assignable secondary literature</td>
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**2.11 OXIDIZING PROPERTIES**

**2.12 DISSOCIATION CONSTANT**

**2.13 VISCOSITY**

<table>
<thead>
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<th>Method</th>
<th></th>
</tr>
</thead>
</table>

30 UNEP PUBLICATIONS
OECD SIDS

TRIETHYL PHOSPHITE

2. PHYSICAL-CHEMICAL DATA

ID: 122-52-1

DATE: 12.01.2005

<table>
<thead>
<tr>
<th>Year</th>
<th>1971</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLP</td>
<td></td>
</tr>
<tr>
<td>Test substance</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result</th>
<th>0.746 mPas at 13°C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.657 mPas at 25°C</td>
</tr>
<tr>
<td></td>
<td>0.473 mPas at 55°C</td>
</tr>
<tr>
<td></td>
<td>0.375 mPas at 80°C</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reliability</th>
<th>(2) valid with restrictions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Data from handbook or collection of data</td>
</tr>
</tbody>
</table>

24.01.2003 (11) (12)

<table>
<thead>
<tr>
<th>Value</th>
<th>1 - mPa s (dynamic) at 20 °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result</td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td></td>
</tr>
<tr>
<td>Year</td>
<td>2002</td>
</tr>
<tr>
<td>GLP</td>
<td></td>
</tr>
<tr>
<td>Test substance</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reliability</th>
<th>(4) not assignable</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>secondary literature</td>
</tr>
</tbody>
</table>

28.01.2003 (1)

2.14 ADDITIONAL REMARKS
### 3.1.1 PHOTODEGRADATION

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>air</td>
</tr>
<tr>
<td>Light source</td>
<td></td>
</tr>
<tr>
<td>Light spectrum</td>
<td>nm</td>
</tr>
<tr>
<td>Relative intensity</td>
<td>based on intensity of sunlight</td>
</tr>
<tr>
<td>INDIRECT PHOTOLYSIS</td>
<td></td>
</tr>
<tr>
<td>Sensitizer</td>
<td>OH</td>
</tr>
<tr>
<td>Conc. of sensitizer</td>
<td>500000 molecule/cm³</td>
</tr>
<tr>
<td>Rate constant</td>
<td>0.000000000058 cm³/(molecule*sec)</td>
</tr>
<tr>
<td>Degradation</td>
<td>50 % after 6.6 hour(s)</td>
</tr>
<tr>
<td>Deg. product</td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td>other (calculated): with SRC-AOPWIN v1.90 (2000)</td>
</tr>
<tr>
<td>Year</td>
<td>2002</td>
</tr>
<tr>
<td>Test substance</td>
<td>as prescribed by 1.1 - 1.4</td>
</tr>
<tr>
<td>Remark</td>
<td>The calculated half-life is based on a mean OH radical concentration of 0.5E+6 OH radicals/cm³ with 24 hours/day according to BUA-study accepted standard conditions. Direct photolysis of triethyl phosphite is not expected because the substance does not absorb light at wavelengths &gt; 290 nm.</td>
</tr>
<tr>
<td>Reliability</td>
<td>(2) valid with restrictions accepted calculation method</td>
</tr>
<tr>
<td>Flag</td>
<td>Critical study for SIDS endpoint</td>
</tr>
</tbody>
</table>

### 3.1.2 STABILITY IN WATER

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>abiotic</td>
</tr>
<tr>
<td>t(1/2) pH4</td>
<td>at °C</td>
</tr>
<tr>
<td>t(1/2) pH7</td>
<td>at °C</td>
</tr>
</tbody>
</table>
t1/2 pH9: 5.1 hour(s) at 23 °C
Degradation: 100 % after 20 minute(s) at pH 7 and 23 °C
Deg. product: yes
Year: 2001
GLP: yes
Test substance: other TS: 99.3% purity

Result: At pH 4 triethyl phosphite degrades immediately to diethyl phosphite. At pH 7 triethyl phosphite hydrolyses completely within 20 minutes.

The following degradation products were detected after 3 h:

<table>
<thead>
<tr>
<th>pH</th>
<th>Triethyl phosphite</th>
<th>Diethyl phosphite</th>
<th>Monoethyl phosphite</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>0 %</td>
<td>100 %</td>
<td>0 %</td>
</tr>
<tr>
<td>7</td>
<td>0 %</td>
<td>89.34 %</td>
<td>10.66 %</td>
</tr>
<tr>
<td>9</td>
<td>69.88%</td>
<td>2.35 %</td>
<td>27.77 %</td>
</tr>
</tbody>
</table>

after about 19 h (one measurement):

<table>
<thead>
<tr>
<th>pH</th>
<th>Triethyl phosphite</th>
<th>Diethyl phosphite</th>
<th>Monoethyl phosphite</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>6.6 %</td>
<td>0 %</td>
<td>93.4 %</td>
</tr>
</tbody>
</table>

At pH 9, it could be estimated the half life and the rate constant: $t_{1/2}=5.1$ hours and $k=3.81E-05$ 1/s.

Test condition: The test was performed in buffered solution at pH=4,7,9, 23°C, during a period of at least 3h.
Concentrations tested: 0.17% (at pH=4), 0.19% (pH=7), 0.17% (pH=9).
Analytical method: 31-Phosphor-NMR spectroscopy.

Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
11.02.2003

Type: abiotic
$\tau_{1/2}$ pH4: at °C
$\tau_{1/2}$ pH7: at °C
$\tau_{1/2}$ pH9: at °C
Degradation: 100 % after 3 hour(s) at pH and °C
Deg. product: yes
Method: other: Test on stability in water with phosphor nuclear magnetic resonance
Year: 1993
GLP: no
Test substance: other TS: 97.1% purity

Remark: Preliminary test on stability of tri-and diethyl phosphite in water, as screening information for the fish toxicity test (see chapter 4.1).

Result: Triethyl phosphite
Test concentration (%): 1
Hydrolysis (%): 100
Time (h): 3
Product of hydrolysis: Diethyl phosphite
Another measurement was performed after 22h and triethyl phosphite was
at that time also not detectable (100% hydrolysis after 22h). In both measurements (after 3 and 22h) diethyl phosphite was found as the hydrolysis product.

Diethyl phosphite
Test concentration (%) : 1
Hydrolysis (%) : 14
Time (h) : 95
Product of hydrolysis : not detected

Test condition : Test was conducted with the test substance in pure water, no control of pH.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

Remark : It was determined the hydrolysis rate in acidic, neutral and basic solution. The rate constant was measured at temperatures of 0°C, 10°C and 50°C, 60°C, 80°C, 90°C. It cannot be derived a hydrolysis rate at room temperature. In acidic and neutral solution triethyl phosphite hydrolyses more rapidly than in basic solution. In basic solution the hydrolysis kinetics followed second order equation whereas in acidic and neutral solution the kinetics followed a first order equation. Diethyl phosphite and monoethyl phosphite were detected as products of hydrolysis. Further information about the test conditions, under which the hydrolysis products occur is not given.

Reliability : (4) not assignable
Original reference in Russian (only abstract in English)
3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Remark : not assignable, hydrolysis
Flag : Critical study for SIDS endpoint
23.11.2000

3.3.2 DISTRIBUTION

Remark : not assignable for triethyl phosphite, hydrolysis
Flag : Critical study for SIDS endpoint
22.12.2004

Media : water - air
Method : other (calculation)
Year : 2003

Result : From the estimated water solubility of 15 g/l and the measured vapor pressure of 2.6 hPa, a Henry's law constant of 2.9 Pa*m³/mol can be calculated, indicating a moderate volatility of triethyl phosphite from aqueous solutions. The volatility of the main degradation product under neutral conditions, diethyl phosphite, is slightly lower based on the Henry's law constant of about 1.8 Pa*m³/mol estimated based on a water solubility of 115 g/l and a vapor pressure of 14.9 hPa (data taken from EPIWIN).

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
22.12.2004

Media : air - biota - sediment(s) - soil - water
Method : Calculation according Mackay, Level I
Year : 2003

Remark : Due to hydrolysis the determination of the Henry constant and the environmental distribution according the Mackay Fugacity Model Level I is not applicable for triethyl phosphite. For the main degradation product under environmental pH conditions, diethyl phosphite, the target compartments according to a Mackay level 1 fugacity model are water (61.7 %) and air (38.2 %).

Test condition : Data base for calculation (diethyl phosphite):
  temperature [°C]: 20
  molar mass [g/mol]: 171.05
  vapour pressure [Pa]: 1490 (data taken from EPIWIN)
  water solubility [g/L]: 115 (calculated with WSKOW v1.40)
  log Kow: -0.15 (calculated with KOWWIN v1.66)

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
22.12.2004
3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

<table>
<thead>
<tr>
<th>Type</th>
<th>aerobic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inoculum</td>
<td>predominantly domestic sewage</td>
</tr>
<tr>
<td>Concentration</td>
<td>20 mg/l related to DOC (Dissolved Organic Carbon) related to</td>
</tr>
<tr>
<td>Contact time</td>
<td></td>
</tr>
<tr>
<td>Degradation</td>
<td>69 (±) % after 28 day(s)</td>
</tr>
<tr>
<td>Result</td>
<td>other: not readily biodegradable</td>
</tr>
<tr>
<td>Deg. product</td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td>OECD Guide-line 301 E &quot;Ready biodegradability: Modified OECD Screening Test&quot;</td>
</tr>
<tr>
<td>Year</td>
<td>1993</td>
</tr>
<tr>
<td>GLP</td>
<td>yes</td>
</tr>
<tr>
<td>Test substance</td>
<td>other TS: 98.8 % purity</td>
</tr>
</tbody>
</table>

Remark: Triethyl phosphite reacts within 3h with water to form diethyl phosphite and ethanol. Diethyl phosphite then reacts with water to form monoethyl phosphite and ethanol (see chapter 3.1.2: Stability in Water). In both reactions ethanol is formed which is readily biodegradable. Biodegradation half life of triethyl phosphite: 7 days.

Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
29.10.2002

3.6 BOD5, COD OR BOD5/COD RATIO

Remark: ThOD: 1830 mg/g
3.7 BIOACCUMULATION

**Remark**: not assignable, hydrolysis
23.11.2000

3.8 ADDITIONAL REMARKS
### 4.1 ACUTE/PROLONGED TOXICITY TO FISH

<table>
<thead>
<tr>
<th>Type</th>
<th>static</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
<td>Brachydanio rerio (Fish, fresh water)</td>
</tr>
<tr>
<td>Exposure period</td>
<td>96 hour(s)</td>
</tr>
<tr>
<td>Unit</td>
<td>mg/l</td>
</tr>
<tr>
<td>LC0</td>
<td>120.1</td>
</tr>
<tr>
<td>LC50</td>
<td>251.6</td>
</tr>
<tr>
<td>LC100</td>
<td>526.9</td>
</tr>
<tr>
<td>Limit test</td>
<td>no</td>
</tr>
<tr>
<td>Analytical monitoring</td>
<td>yes</td>
</tr>
<tr>
<td>Method</td>
<td>other: &quot;Acute Toxicity for Fish&quot; (C.1) of the directive 67/548/EEC, Annex V (Draft 1992)</td>
</tr>
<tr>
<td>Year</td>
<td>1993</td>
</tr>
<tr>
<td>GLP</td>
<td>yes</td>
</tr>
<tr>
<td>Test substance</td>
<td>other TS: Triethyl phosphite (98.8%)</td>
</tr>
</tbody>
</table>

**Remark**

A preliminary test (see chapter 3.1.2) showed that the test substance triethyl phosphite hydrolyses completely within 3 hours to diethyl phosphite and diethyl phosphite remains stable (>80% Recovery) for 96 h (duration of the fish test). Diethyl phosphite was followed analytically in place of triethyl phosphite during the study. Analytical monitoring: GC.

In order to ensure that hydrolysis of triethyl phosphite to diethyl phosphite was largely complete, the test started 2 hours after inserting the test substance, i.e. measurement of abiotic parameters; sampling for accompanying analysis; introducing of test fish.

The GC-analysis showed that the measured concentrations of diethyl phosphite at test start were about 60 % of the concentration that could be calculated from the triethyl phosphite concentration assuming full hydrolysis. Within the first 24 h the concentrations further decreased and remained then nearly constant throughout the test. As the measured diethyl phosphite concentrations were lower than the calculated nominal values, the test results are based on measured diethyl phosphite concentrations.

**Result**

The above given results (LC0,LC50,LC100) are estimated values related to triethyl phosphite, and are based on those concentrations reported in the original study: effect concentrations for diethyl phosphite, the degradation product.

The following results related to diethyl phosphite are given in the original study:

<table>
<thead>
<tr>
<th>LC0</th>
<th>99.8 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>LC100</td>
<td>438 mg/l</td>
</tr>
<tr>
<td>LC50: Geometric mean between LC0 and LC100</td>
<td>209.1 mg/l</td>
</tr>
</tbody>
</table>

**Test condition**

- 7-months-old fishes were used. Length: 2.5 to 3.5 cm
- Tank: 300 x 135 x 200 mm; 5l test medium, synthetic origin, prepared according to ISO; no replicates
- Initial concentrations were analytically checked every 24 h with GC
- Concentrations tested: 250, 354, 500, 707, 1000 mg/l
- Temperature during the test: all tests reported the temperature in the range of 20.9 to 22.6 °C
- Oxygen concentration: during the test oxygen did not sink below 84% of the saturation level.
- pH: at the start of the test the pH was 7.4-7.8, in the middle of the test was reported to be 5.4-5.5 remaining in this pH-range till the end of the test.

**Reliability**

(1) valid without restriction
4. ECOTOXICITY

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

**Type**: static

**Species**: Daphnia magna (Crustacea)

**Exposure period**: 24 hour(s)

**Unit**: mg/l

**EC0**: 26.5

**EC50**: 94.1

**EC100**: 426

**Limit Test**: no

**Analytical monitoring**: no

**Method**: other: UBA-Verfahrensvorschlag: "Bestimmung der Schwimmunfähigkeit beim Wasserfloh Daphnia magna, EC0, EC50, EC100; 24h, static" (Mai 1984)

**Year**: 1989

**GLP**: yes

**Test substance**: other TS: Diethyl phosphite (98.7%)

**Remark**: A stock solution with 500 mg/l diethyl phosphite was prepared and stirred for 3 hours with a magnetic stirrer at 50 °C. Stability of diethyl phosphite over a 24 hours period was demonstrated in a preliminary test for an acute toxicity test with fish (see chapter 4.1).

**Result**: The above given results (LC0, LC50, LC100) are estimated values related to triethyl phosphite, and are based on those concentrations reported in the original study: effect concentrations for diethyl phosphite, the degradation product. The following results related to diethyl phosphite are given in the original study:

- **LC0**: 22 mg/l
- **LC100**: 354 mg/l
- **LC50** was calculated using the Probit Analysis. **LC50**: 78.2 mg/l

**Test condition**: - 6 to 24-hours-old daphnids.
- Test vessel: cylindric 4 x 6.5 cm; 20ml test medium, natural origin: filtered shallow water. 10 daphnias/vessel; 2 replicates per concentration level.
- Reference substance: Potassium dichromate
- Initial concentrations were analytically checked every 24 h
- Concentrations tested: 5.5, 11, 22, 44, 88, 177, 354 mg/l
- Temperature at the end of the test: 19.1-19.4 °C
- Oxygen concentration at the end of the test: 8.2-8.4 mg/l
- pH at the end of the test: 8 to 6.9 depending on the applied initial concentration.
- The starting test conditions were as prescribed in the national guideline.

**Reliability**: (2) valid with restrictions

Test procedure in accordance with national standard method with acceptable restrictions

**Flag**: Critical study for SIDS endpoint (17)
4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

<table>
<thead>
<tr>
<th>Species</th>
<th>Scenedesmus subspicatus (Algae)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endpoint</td>
<td>growth rate</td>
</tr>
<tr>
<td>Exposure period</td>
<td>72 hour(s)</td>
</tr>
<tr>
<td>Unit</td>
<td>mg/l</td>
</tr>
<tr>
<td>NOEC</td>
<td>= 37</td>
</tr>
<tr>
<td>EC50</td>
<td>&gt; 73.6</td>
</tr>
<tr>
<td>Limit test</td>
<td>no</td>
</tr>
<tr>
<td>Analytical monitoring</td>
<td>yes</td>
</tr>
<tr>
<td>Method</td>
<td>other: &quot;Growth Inhibition Test for Algae&quot; (C.3) of the directive 92/69/EEC, Annex V (1992)</td>
</tr>
<tr>
<td>Year</td>
<td>1999</td>
</tr>
<tr>
<td>GLP</td>
<td>yes</td>
</tr>
<tr>
<td>Test substance</td>
<td>other TS: Triethyl phosphite (98.8%)</td>
</tr>
</tbody>
</table>

Remark:
For the performance of this test, the results of the preliminary test before testing fish toxicity (see chapter 4.1) were taken into account: the test substance triethyl phosphite hydrolyses completely within 3 hours to diethyl phosphite and diethyl phosphite remains stable for 72 h (duration of algae test).

Analytical monitoring: TOC-measurement (1 mg/l TOC corresponds to 2.9 mg/l diethyl phosphite).
In order to ensure that hydrolysis of triethyl phosphite to diethyl phosphite was almost complete, the test started 2 hours after inserting the test substance, i.e. measurement of abiotic parameters; sampling for accompanying analysis; introducing of test inoculum.

Result:
The above given results (NOEC,EC50) are estimated values related to triethyl phosphite.
The following results related to diethyl phosphite are given in the original study:
- Endpoint biomass and growth rate:
  - EC50: > 92.8 mg/l
- The NOEC/LOEC values were calculated in the original study using the Dunnnett's test related to the parameter cell number:
  - NOEC: >= 92.8 mg/l
  - LOEC: > 92.8 mg/l
- Based on the original data, the NOEC/EC50 of growth rate and biomass for triethyl phosphite can be calculated (using either William's or Dunnnett's test) to:
  - NOEC: 37 mg/l
  - EC50: > 73.6 mg/l
- For diethyl phosphite the corresponding data are:
  - NOEC: 30.8 mg/l
  - EC50: > 61.2 mg/l

Test condition:
Test conditions followed the EU-guideline given above. In the following are given some characteristics about the test system:
- Erlenmeyer flask of 300 ml with 100ml test medium: deionised water. Ca.43300 cells/ml were injected. No replicates.
- Initial concentrations were analytically checked at the beginning and at the end of the test by measuring TOC.
- Concentrations tested: 2.8, 5.6, 11.25, 22.5, 45, 90 mg/l.
- Temperature was during the tests in the range of 21-25°C.
- Oxygen concentration was not controlled.
- pH was approx. 8 at the beginning and 10 at the end of the test.

Reliability:
(1) valid without restriction
Guideline study

Flag:
Critical study for SIDS endpoint
4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type: aquatic
Species: activated sludge
Exposure period: 3 hour(s)
Unit: mg/l
EC50: 4720
Analytical monitoring: no
Method: other: "Test for Inhibition of Oxygen Consumption by Activated Sludge" ISO 8192 (1986)
Year: 1993
GLP: yes
Test substance: other TS: 97.1% purity

Remark: Concentrations tested: 1000, 1800, 3200, 5600, 10000 mg/l.
Reference-substance: 3,5-Dichlorophenol.
Result: EC50: arithmetic mean of the tested nominal concentrations.
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS
5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

<table>
<thead>
<tr>
<th>Type</th>
<th>LD50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>&gt; 2385 mg/kg bw</td>
</tr>
<tr>
<td>Species</td>
<td>rat</td>
</tr>
<tr>
<td>Strain</td>
<td>no data</td>
</tr>
<tr>
<td>Sex</td>
<td>male</td>
</tr>
<tr>
<td>Number of animals</td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td>other: no data, the test substance was administered as an &quot;oily solution&quot;</td>
</tr>
<tr>
<td>Doses</td>
<td>other: 1 and 2.5 mL/kg bw (approx. 954 and 2385 mg/kg bw)</td>
</tr>
<tr>
<td>Method</td>
<td>other: see remark</td>
</tr>
<tr>
<td>Year</td>
<td>1959</td>
</tr>
<tr>
<td>GLP</td>
<td>no</td>
</tr>
<tr>
<td>Test substance</td>
<td>other TS: Trietyhlphosphite, purity not stated</td>
</tr>
</tbody>
</table>

Result

- mortality:
  - 954 mg/kg bw: 0/3
  - 2385 mg/kg bw: 0/3
- Clinical signs: no symptoms observed
- no further detail reported

Test condition

- treatment by single gavage; 3 animals / dose;
- dosing volume: not reported;
- doses: 1 and 2.5 ml/kg (specific gravity: 0.954g/cm3)
- post-exposure observation period: not reported
- no further detail reported

Reliability

- (2) valid with restrictions
- limited documentation.

Flag

- 29.04.2003: Critical study for SIDS endpoint (19)

<table>
<thead>
<tr>
<th>Type</th>
<th>LD50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>1840 - 2470 mg/kg bw</td>
</tr>
<tr>
<td>Species</td>
<td>rat</td>
</tr>
<tr>
<td>Strain</td>
<td>Fischer 344</td>
</tr>
<tr>
<td>Sex</td>
<td>male/female</td>
</tr>
<tr>
<td>Number of animals</td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td>other: corn oil</td>
</tr>
<tr>
<td>Doses</td>
<td>1000, 1500, 2000, 2500, 3000 and 4000 mg/kg bw;</td>
</tr>
<tr>
<td>Method</td>
<td>other: see test condition</td>
</tr>
<tr>
<td>Year</td>
<td>1986</td>
</tr>
<tr>
<td>GLP</td>
<td>no data</td>
</tr>
<tr>
<td>Test substance</td>
<td>other TS: Triethylphosphite, purity not stated</td>
</tr>
</tbody>
</table>

Result

- LD50 males: 2470 (2220-2730) mg/kg;
- LD50 females: 1840 (1620-2140) mg/kg;
- oral doses produced rapid breathing and tremors prior to death; most deaths occurred within 24 hours of dosing; survivors gained weight during observation period
- no further detail reported
Test condition: ANIMALS: Fischer 344 rats; 10 animals/sex/dose; DOSING: the test substance was mixed with Mazola corn oil and administered at constant volumes of 1% body weight. OBSERVATION PERIOD: 14 days
PARAMETERS: mortality, observation
METHOD: animals were fasted prior to dosing;
LD50 was calculated according probit method of Finney

Reliability: (2) valid with restrictions
limited documentation

Flag: 30.04.2003
Critical study for SIDS endpoint

Type: LD50
Value: 3720 - 3800 mg/kg bw
Species: mouse
Strain: male/female
Number of animals:
Vehicle: other: corn oil
Doses: 2000, 3000, 3500, 4000, 4500, 5000 mg/kg bw

Method: other: see test condition
Year: 1986
GLP: no data
Test substance: other TS: Triethylphosphite, purity not stated

Result: LD50:
males: 3720 (3190-4270) mg/kg bw;
females: 3800 (3460-4110) mg/kg bw;
OBSERVATION:
oral doses produced rapid breathing and tremors prior to death; most deaths occurred within 24 hours of dosing; survivors gained weight during observation period
no further detail reported

Test condition: ANIMALS: CD-1 mice; 10 animals/sex/dose;
METHOD: animals were fasted prior to dosing;
DOSING: the test substance was mixed with Mazola corn oil and administered at constant volumes of 1% body weight.

Reliability: (2) valid with restrictions
limited documentation

Flag: 30.04.2003
Critical study for SIDS endpoint

Type: LD50
Value: 4000 mg/kg bw
Species: rat
Strain: Wistar
Sex:
Number of animals:
Vehicle:
Doses:
Method:
Year: 1978
GLP: no
Test substance:
### 5. TOXICITY

#### 5.1.2 ACUTE INHALATION TOXICITY

<table>
<thead>
<tr>
<th>Type</th>
<th>LC50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>$= 11063 - 11620$ mg/m³</td>
</tr>
<tr>
<td>Species</td>
<td>rat</td>
</tr>
<tr>
<td>Strain</td>
<td>Fischer 344</td>
</tr>
<tr>
<td>Sex</td>
<td>male/female</td>
</tr>
<tr>
<td>Number of animals</td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td>other: undiluted</td>
</tr>
<tr>
<td>Doses</td>
<td>not reported</td>
</tr>
<tr>
<td>Exposure time</td>
<td>6 hour(s)</td>
</tr>
<tr>
<td>Method</td>
<td>other: see remark</td>
</tr>
<tr>
<td>Year</td>
<td>1986</td>
</tr>
<tr>
<td>GLP</td>
<td>no data</td>
</tr>
<tr>
<td>Test substance</td>
<td>other TS: Triethylphosphite, purity not stated</td>
</tr>
</tbody>
</table>

Remark: No data are available regarding the stability of the aerosol under the conditions of the test.

Result: LC50

- males: $11,620$ (10,083-12,761) mg/m³; females: $11,063$ mg/m³ (confidence limits could not be calculated due to reversals in mortality curve);

**OBSERVATION:**

- signs of toxic stress included eye and upper respiratory irritation, salivation and rapid, shallow breathing; most deaths occurred within 24 hours following treatment; subnormal weight gain of survivors during the 14-days observation period; surviving animals appeared normal to conclusion of
observation period
NECROPSY:
dead animals: restricted to diffuse lung congestion;

no further detail reported

Test condition:
ANIMALS: 10 rats/sex/group
Fischer 344 rats; age: 9-11 weeks; 10 males and 10 female per group

METHOD:
exposure MMAD’s were between 1.6 and 3.5µm; aerosol concentrations were produced using a Solosphere (R) nebulizer; analysis by GC; aerosol measurement by cascade impactor; observation period: 14 days

No data on type of exposure (nose only/whole body)
No information is available as to the stability under the conditions of aerosol generation

Reliability:
(2) valid with restrictions
Exposure levels not reported

Flag:
Critical study for SIDS endpoint

03.03.2004

Type:
LC50

Value:
= 6203 - 9164 mg/m³

Species:
mouse

Strain:
CD-1

Sex:
male/female

Number of animals:

Vehicle:
other: undiluted

Doses:
not reported

Exposure time:
6 hour(s)

Method:

Year:
1986

GLP:
no data

Test substance:
other TS: Triethylphospite, purity not stated

Method:
CD-1 mice; age: 9-11 weeks; 10 animals/sex/concentration;

RESULT:
LC50:
males: 6,203 mg/m3; LC50 females: 9,164 (8,821-9,469) mg/m3; ; (confidence limits could not be calculated in males due to reversals in mortality curve)

OBSERVATION:
signs of toxic stress included eye and upper respiratory irritation, salivation and rapid, shallow breathing; most deaths occurred within 24 hours following treatment; subnormal weight gain of survivors during the 14-days observation period; surviving animals appeared normal to conclusion of observation period

NECROPSY:
dead animals: restricted to diffuse lung congestion;

Reliability:
(2) valid with restrictions
### 5.1.3 ACUTE DERMAL TOXICITY

<table>
<thead>
<tr>
<th>Type</th>
<th>LD50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>2800 - 3000 mg/kg bw</td>
</tr>
<tr>
<td>Species</td>
<td>rabbit</td>
</tr>
<tr>
<td>Strain</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>male/female</td>
</tr>
<tr>
<td>Number of animals</td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td>other: undiluted</td>
</tr>
<tr>
<td>Doses</td>
<td>2.0, 2.5 and 3.0 g/kg bw</td>
</tr>
<tr>
<td>Method</td>
<td>other: see Test Condition</td>
</tr>
<tr>
<td>Year</td>
<td>1986</td>
</tr>
<tr>
<td>GLP</td>
<td>no data</td>
</tr>
<tr>
<td>Test substance</td>
<td>other TS: Triethylphosphite, purity not stated</td>
</tr>
</tbody>
</table>

**Result**: 
LD50 males: 2800 mg/kg; LD50 females: >3000 mg/kg

no further detail reported

**Test condition**: 
**ANIMALS**: New Zealand White Rabbits; weight 2-3kg; 5 animals/sex/dose; 

METHOD: compound applied to an area approx. 30% total body surface; covered with gauze bandage, plastic wrap, and elastic tape; removed covers after 24 h, wiped clean, and observed for 14 days; LD50 was calculated according probit method of Finney

**Reliability**: 
(2) valid with restrictions limited documentation

**Flag**: Critical study for SIDS endpoint (20)

---

### Additional Data

<table>
<thead>
<tr>
<th>Type</th>
<th>LD50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>&gt; 954 mg/kg bw</td>
</tr>
<tr>
<td>Species</td>
<td>rat</td>
</tr>
<tr>
<td>Strain</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>male</td>
</tr>
<tr>
<td>Number of animals</td>
<td>2</td>
</tr>
<tr>
<td>Vehicle</td>
<td>other: undiluted</td>
</tr>
<tr>
<td>Doses</td>
<td>1 ml/kg (954 mg/kg bw)</td>
</tr>
<tr>
<td>Method</td>
<td>other: see Test Condition</td>
</tr>
<tr>
<td>Year</td>
<td>1959</td>
</tr>
<tr>
<td>GLP</td>
<td>no</td>
</tr>
<tr>
<td>Test substance</td>
<td>other TS: Triethylphosphite, purity not stated</td>
</tr>
</tbody>
</table>

**Result**: 
mortality: 0/2; no symptoms observed; no irritation of skin

no further detail reported

**Test condition**: undiluted test substance was applied for 2 hours on an area of 15 cm² on the abdomen of animals; after application test substance was removed by solvent
It is not reported whether the test substance was applied under open, semi-
5.1.4 ACUTE TOXICITY, OTHER ROUTES

<table>
<thead>
<tr>
<th>Type</th>
<th>LD50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>1500 mg/kg bw</td>
</tr>
<tr>
<td>Species</td>
<td>rat</td>
</tr>
<tr>
<td>Strain</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Number of animals</td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td></td>
</tr>
<tr>
<td>Doses</td>
<td></td>
</tr>
<tr>
<td>Route of admin.</td>
<td>i.p.</td>
</tr>
<tr>
<td>Exposure time</td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td></td>
</tr>
<tr>
<td>Year</td>
<td>1978</td>
</tr>
<tr>
<td>GLP</td>
<td>no</td>
</tr>
<tr>
<td>Test substance</td>
<td></td>
</tr>
</tbody>
</table>

Reliability : (4) not assignable
insufficient detail reported to allow assessment

17.01.2003 (21)

<table>
<thead>
<tr>
<th>Type</th>
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</thead>
<tbody>
<tr>
<td>Value</td>
<td>&gt; 5000 mg/kg bw</td>
</tr>
<tr>
<td>Species</td>
<td>mouse</td>
</tr>
<tr>
<td>Strain</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Number of animals</td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td></td>
</tr>
<tr>
<td>Doses</td>
<td></td>
</tr>
<tr>
<td>Route of admin.</td>
<td>i.p.</td>
</tr>
<tr>
<td>Exposure time</td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td></td>
</tr>
<tr>
<td>Year</td>
<td></td>
</tr>
<tr>
<td>GLP</td>
<td>no data</td>
</tr>
<tr>
<td>Test substance</td>
<td></td>
</tr>
</tbody>
</table>

Reliability : (4) not assignable
LD 50 only, no further detail; secondary citation

17.01.2003 (23)

5.2.1 SKIN IRRITATION

| Species | rabbit |
| Concentration | 100 % |
| Exposure   | Semiocclusive |
| Exposure time | 4 hour(s) |
| Number of animals | 6 |
Vehicle : other: undiluted
PDII : 1.4
Result : slightly irritating
Classification :
Method : other: OECD Guide-line 4041980
Year : 1982
GLP : no
Test substance : other TS: Triethylphosphite, purity not stated

Result : All six4 animals showed slight or clearly visible erythema (grade 1 or 2) up to 48 hours. At day 7, slight erythema (grade 1) still persisted in 5 animals, but had resolved in all but one animal at day 10.
None of the animals showed edema at any of the observations

Test condition : TEST ANIMALS: 6 female HC:NZW rabbits, mean weight: 3.5 kg
EXPOSURE TO TEST SUBSTANCE: 0.5 mL undiluted test substance was applied on a gauze pad (2.5 x 2.5 cm) under semi-occlusive conditions to the intact skin. After the end of the exposure time the application sites were washed with water.
Skin effects were scored according to the Draize system at 1, 24, 48, 72 hours and at 7 and 10 days after the end of the exposure.

Reliability : (2) valid with restrictions
purity of test substance not reported; short post-exposure observation period
Flag 27.01.2003 : Critical study for SIDS endpoint
(24)

Species : rabbit
Concentration :
Exposure :
Exposure time : 4 hour(s)
Number of animals :
Vehicle :
PDII :
Result : slightly irritating
Classification :
Method : other: application on ear
Year : 1959
GLP :
Test substance :

Reliability : (2) valid with restrictions
non standard application site
Flag 20.01.2003 : Critical study for SIDS endpoint
(19)

Species : rabbit
Concentration :
Exposure :
Exposure time :
Number of animals :
Vehicle :
PDII :
Result : slightly irritating
Classification :
Method :
Year : 1978
GLP : no
5.2.2 EYE IRRITATION

**Species:** rabbit

**Concentration:** 100% 

**Dose:** 0.1 ml

**Exposure time:** 24 hour(s)

**Comment:** rinsed after (see exposure time)

**Number of animals:** 3

**Vehicle:**

**Result:** slightly irritating

**Classification:** OECD Guide-line 405 "Acute Eye Irritation/Corrosion"

**Year:** 1982

**GLP:** no

**Test substance:** other TS: Triethylphosphite, purity not stated

**Result:** 1 hour after application: all three animals showed erythema (grade 1 or 2) and two of them also chemosis (grade 1); 24 hours after application: two animals showed erythema (grade 1)
All effects were completely reversible within 48 hours. No effects were noted in corneas and irises at any observation.

**Test condition**
- **TEST ANIMALS:** 3 male HC:NZW rabbits, mean weight 3.5 kg.
- 24 hours after instillation of the test substance, the treated eyes were washed with physiological saline.
- Observations at 1, 24, 48 and 72 hours and at 7 days after instillation of the test substance. Scoring was performed according to the Draize scheme.

**Reliability**
- (2) valid with restrictions
- purity of test substance not stated

**Flag**
- Critical study for SIDS endpoint

**Species**
- rabbit

**Concentration**
- :

**Dose**
- :

**Exposure time**
- :

**Comment**
- :

**Number of animals**
- :

**Vehicle**
- :

**Result**
- slightly irritating

**Classification**
- :

**Method**
- :

**Year**
- 1978

**GLP**
- no

**Test substance**
- :

**Reliability**
- (4) not assignable
- insufficient detail reported to allow assessment

**Species**
- rabbit

**Concentration**
- undiluted

**Dose**
- .1 ml

**Exposure time**
- :

**Comment**
- :

**Number of animals**
- 9

**Vehicle**
- :

**Result**
- moderately irritating

**Classification**
- :

**Method**
- Draize Test

**Year**
- 1986

**GLP**
- no data

**Test substance**
- other TS: Triethylphosphite, purity not stated

**Result**
- irritating effects only observed on day 1, independent of washing
- Effects after washing were more severe than without washing. The following Draize scores are reported:
  - unwashed (6 rabbit mean): 1d - 6.0, 2 d - 0.0, 3 d - 0.0, 4 d - 0.0, 7d - 0.0
  - washed (3 rabbit mean): 1 d - 8.0, 2 d - 0.0, 3 d - 0.0, 4 d - 0.0, 7d - 0.0

**Test condition**
- **ANIMALS:**
  - New Zealand White, 6+3 females, 2-3 kg
- **METHOD:**
  - A topical anesthetic was instilled in all rabbit eyes approximately 2 minutes prior to treatment.
  - 0.1 mL of undiluted test substance was instilled into the conjunctival sac, the contralateral eye served as untreated control.
  - 3 animals were washed for 1 minute with lukewarm water 20 to 30 sec after
5.3 SENSITIZATION

Type: Guinea pig maximization test
Species: guinea pig
Concentration:
1st: Induction 5% intracutaneous
2nd: Induction 100% occlusive epicutaneous
3rd: Challenge 100% occlusive epicutaneous
Number of animals: 50
Vehicle: other: peanut oil (pharmaceutical grade)
Result: sensitizing
Classification: OECD Guide-line 406 "Skin Sensitization"
Method: yes
Year: 1993
GLP: yes
Test substance: other TS: purity 98.8%

Result: 19 out of 20 animals showed positive results at 48 hours after challenge with the undiluted test material. None of the negative control animals showed any positive effects.

Test condition: TEST ANIMALS: Bor:DHPW guinea pigs, mean weight 327 g, age 5-7 weeks.
TEST CONCENTRATIONS for the main study were determined from the results of a pre-study on the irritation threshold, performed with 50 male animals.

Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
27.01.2003

5.4 REPEATED DOSE TOXICITY

Type:
Species: rat
Sex: male
Strain: no data
Route of admin.: gavage
Exposure period: 14 days
Frequency of treatm.: daily
Post exposure period: 3 Weeks
Doses: 0.2 ml/kg bw
Control group: other: no data
Method: Year: 1959
GLP: no
Test substance: other TS: Triethylphosphite, no further data

Method: 10 male rats were treated daily with 0.2 ml/kg bw for 14 days and observed afterwards for an unspecified time
Result: no clinical signs of toxicity
Reliability: (4) not assignable
insufficient detail reported to allow assessment

27.01.2003

Type: rat
Species: male/female
Sex: Wistar
Strain: gavage
Route of admin.: 32 days
Exposure period: daily
Frequency of treatm.: no
Post exposure period: no
Doses: 0, 30, 150, or 750 mg/kg bw
Control group: yes, concurrent vehicle
NOAEL: 150 mg/kg bw
Method: OECD Guide-line 407 "Repeated Dose Oral Toxicity - Rodent: 28-day or 14-d Study"
Year: 1992
GLP: yes
Test substance: other TS: purity 98.8%

Result: Clinical findings, mortality:
750 mg/kg bw: impaired general condition, emaciation, unkempt fur, increased mortality (1 male and 1 female; another female was killed in moribund state,)
No effects on mortality were seen at 150 mg/kg bw.

Body weight, food consumption, water consumption:
750 mg/kg bw: reduction of all 3 parameters (body weight gain: - 37% (males), - 13% (females); food consumption: - 29% (males), - 15% (females); water consumption: - 28% (males), - 12% (females).
No effect on body weight gain, food and water consumption was noted at 150 mg/kg bw.

Hematology: 750mg/kg, males only:
statistically significant increases in: RBC, Hb, Hct, and granulocyte counts, decreases in: MCH, MCV, and lymphocytes.
No relevant changes were found in males at 150 mg/kg bw and in females at any dose group with the exception of one single female of the 150 mg/kg bw group showing anisocytosis and changes in red and white blood cells
which were interpreted as a chance event by the study authors.

Clinical chemistry:
750 mg/kg bw: increases in alkaline phosphatase activity (males only), and decreases of plasma albumin (both sexes) and triglyceride concentrations (males only).
150 mg/kg bw: no relevant findings

Urinalysis:
750 mg/kg bw: reduced urine volume in males;
150 mg/kg bw: no relevant findings

Necropsy:
750 mg/kg bw: lungs: brown stains in all animals that survived to the end of the study. The male that had died during the study showed dark lungs and yellow spots in the epididymides.

Organ weights:
750 mg/kg bw: increases in relative: lung weights (males: +65%, females +69% as compared to the controls) and in absolute lung weights in females (+46%). Increases in relative adrenal weights (+33% in males, +30% in females), in relative kidney weights (+32% in males, +17% in females), and in relative liver weights (females only, +17%).
150 mg/kg bw: no effect on organ weights

Histopathology:
750 mg/kg bw:
lungs: focal inflammation (all males, 4 females), and fibrosis (4 males, 4 females); hyperplasia of bronchial epithelium in all animals;
Foreign material was found in the lungs of 3/10 animals. In the animal that died during the study, sperm granulomas were noted in the epididymides.
150 mg/kg bw: no pathological changes.
30 mg/kg bw: foreign material was found in the lung of a single animal, together with a minimal inflammatory response in the lung. As this effect was not noted in any other animal of this dose group the study authors assumed that it might have been caused by aspiration following an error in the gavage procedure.

Test condition:
according to Guideline: OECD 407 (1981)

ANIMALS: 5 Wistar rats /sex/group

VEHICLE: polyethylene glycol 400 (Lutrol)

DOSING VOLUME : 5 mL/kg bw

PARAMETERS:
Clinical findings, mortality, body weight, food consumption, water consumption

Hematology:
RBC, Hb, Hct, WBC, MCH, MCHC, MCV, Plateletts, differential WBC, coagulation

Clinical chemistry:
Alkaline phosphatase, ASAT, ALAT, Glucose, bilirubin, cholesterol, triglycerides, creatinine total protein, urea, albumen, phosphate, calcium, chloride

Urinalysis:
spec. gravity, volume, bilirubin, blood, Hb, ketones, pH, protein, sediment
Necropsy:
gross necropsy with collection of >50 tissues
Organ weights:
brain, heart, testes, liver, lung, kidney, spleen, adrenal gland

Histopathology:
heart, liver, spleen, kidney, adrenals of control and high dose animals;
lungs of all animals; all macroscopically altered tissues

Neurotoxicity: not determined

Statistical Method:
Mann-Whitney U-test at significance levels of $p = 0.05$ and $0.01$

Reliability:
(2) valid with restrictions
study performed according to the outdated OECD guideline, e.g. limited
range of tissues examined histopathologically, no investigation of
neurotoxicity was performed in this study

Flag:
Critical study for SIDS endpoint

5.5 GENETIC TOXICITY ‘IN VITRO’

<table>
<thead>
<tr>
<th>Type</th>
<th>Ames test</th>
</tr>
</thead>
<tbody>
<tr>
<td>System of testing</td>
<td>S. typhimurium TA98, 100, 1535, 1537</td>
</tr>
<tr>
<td>Test concentration</td>
<td>20; 100; 500; 2500; 12500 µg/plate (first test); 775; 1550; 3100; 6200; 12400 µg/plate for the repeat test</td>
</tr>
<tr>
<td>Cycotoxic concentr.</td>
<td>&gt; 775 µg/plate</td>
</tr>
<tr>
<td>Metabolic activation</td>
<td>with and without</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
<tr>
<td>Method</td>
<td>other: according Ames</td>
</tr>
<tr>
<td>Year</td>
<td>1988</td>
</tr>
<tr>
<td>GLP</td>
<td>yes</td>
</tr>
<tr>
<td>Test substance</td>
<td>other TS: purity 99.45%</td>
</tr>
</tbody>
</table>

Remark:
The positive controls were functional

Result:
None of the tested strains showed a dose-related and biologically relevant
increase in mutant counts over those of the negative controls, both with
and without the metabolic activation.

Test condition:
Metabolic activation: Rat liver S9-mix from Aroclor 1254 induced rats.
plate incorporation assay
VEHICLE: DMF
NEGATIVE CONTROL: DMF
POSITIVE CONTROLS:
without S-9: sodium azide (10 µg/plate), nitrofurantoin (0.2 µg/plate), 4-
nitro-1,2-phenylene-diamine (10 µg/plate),
with S-9: 2-aminoanthracene (3 µg/plate)
EVALUATION CRITERIA: a reproducible and dose-related increase (i.e.
greater than twice the negative control count) in mutant counts for at least
one strain was considered a positive result.
STATISTICAL METHOD: not performed.
An independent repeat experiment was performed.

Reliability:
(2) valid with restrictions
only 4 tester strains used, no "untreated" negative control was used;
cultures treated with the vehicle (dimethylformamide; DMF) were used as
"negative control". No additional cultures were used which were exposed to
the culture medium alone, i.e. without addition of the vehicle
5. TOXICITY

5.6 GENETIC TOXICITY 'IN VIVO'

| Flag | 17.08.2004 | Critical study for SIDS endpoint |

Type: Micronucleus assay
Species: mouse
Sex: male/female
Strain: NMRI
Route of admin.: i.p.
Exposure period: single i.p. injection
Doses: 1500 mg/kg
Result: negative
Method: OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year: 1992
GLP: yes
Test substance: other TS: purity 98.8%

Remark:
In a pre-test groups of five females and five males were intraperitoneally administered with 1000 mg/kg bw, 1500 mg/kg bw, 1750 mg/kg bw and 2500 mg/kg bw triethyl phosphite dissolved in corn oil. The following symptoms were recorded up to 48 hours, starting at exposure levels of 1000 mg/kg bw: apathy, semianaesthetised state, roughened fur, staggering gait, sternal and lateral recumbency, spasm, twitching, shivering, difficulty in breathing and flat breathing. In addition, 2 of 5 animals died in the 1750 mg/kg bw group, and 4 out of 5 animals in the 2500 mg/kg bw group. As the test substance was shown to be not stable in corn oil at a concentration of 10 mg/mL, an additional study was performed with paraffinum perliquidum as vehicle. In this study no animal died after a single intraperitoneal dose of 1500 mg/kg bw. The following symptoms were recorded for up to 48 hours: apathy, roughened fur, staggering gait, sternal and lateral recumbency, spasm, shivering and difficulty in breathing.

Result:
TOXICITY:
All treated animals showed the following symptoms of toxicity after administration of 1500 mg/kg bw triethyl phosphite until sacrifice: apathy, semi-anæsthetised state, roughened fur, pallor, staggering gait, sternal position, spasm, twitching, shivering and difficulty in breathing. No symptoms were recorded for the control group. All animals survived until the end of the test. There was an altered ratio between normochromatic and polychromatic erythrocytes with relevant variations noted for the 16 hours group.

CLASTOGENICITY:
no effect; there were also no relevant variations in results between males and females.

The ratio of polychromatic to normochromatic erythrocytes was altered by the treatment with triethyl phosphite in the 16-hours group as shown in the following:
Negative control: 1000:711;
Triethyl phosphite: 1000:1450 (16 hours group);
Triethyl phosphite: 1000:940 (24 hours group);
Triethyl phosphite: 1000:1004 (48 hours group);
Positive control: 1000:680

There was no increase in the incidence of micronucleated polychromatic erythrocytes in the triethyl phosphite treated groups, whereas the positive
control showed a significant increase:
Negative control: 2.0 +/- 1.3 / 1000;
Triethyl phosphate: 2.3 +/- 1.6 / 1000 (16 hours group);
Triethyl phosphate: 2.2 +/- 1.9 / 1000 (24 hours group);
Triethyl phosphate: 2.5 +/- 1.9 / 1000 (48 hours group);
Positive control: 15.9 +/- 5.9 / 1000

Test condition:
TEST ANIMALS: young adult male and virgin female NMRI mice
(Bor:NMRI), weighing between 29 and 42 grams at study begin (age
between 8 and 12 weeks). 5 males and 5 females were used per group.
EXPOSURE: Animals were dosed intraperitoneally with the test substance
dissolved in paraffinum perliquidum and sacrificed 16 hours, 24 hours or 48
hours after the administration.
DOSING VOLUME: 5 mL/kg bw (10 mL/kg bw in the positive controls)
POSITIVE CONTROL: cyciophosphamid, 20 mg/kg bw, dissolved in
deonised water, intraperitoneally. Animals were sacrificed 24 hours after
the administration.
PREPARATION OF SPECIMENS: at least one intact femur was prepared
from each sacrificed animal, and smears were prepared according to the
EVALUATION: Coded slides were evaluated using light microscopy.
Generally, 1000 polychromatic erythrocytes were counted per animal. The
incidence of cells with micronuclei was determined, as well as the ratio
of polychromatic to normochromatic erythrocytes (number of normochromatic
erythrocytes per 1000 polychromatic ones). In addition, also the number
of micronucleated normochromatic erythrocytes was determined.
STATISTICAL METHODS: Standard deviation, Wilcoxon’s non-parametric
rank sum test at a 5% significance level, or one-sided chi-square-test, if the
micronulei rate for polychromatic erythrocytes was increased in the
negative controls.
ASSESSMENT CRITERIA: a result was considered positive if, at any of the
intervals, there was a relevant and significant increase in the number of
polychromatic erythrocytes showing micronuclei in comparison to the
negative control. A test was considered negative if there was no relevant or
significant increase in the rate of micronucleated polychromatic
erythrocytes at any time. A test was also considered negative if there was
no significant increase in that rate which according to the laboratory’s
experience was within the range of negative controls.
ACCEPTANCE CRITERIA: a test was considered acceptable if the figures
of negative and positive controls were within the expected range, in
accordance with the laboratory’s experience and/or the available literature
data.

Conclusion:
Triethyl phosphate did not induce micronuclei after a single intraperitoneal
injection of 1500 mg/kg bw in mice.

Reliability:
(1) valid without restriction
Flag:
Critical study for SIDS endpoint

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Type: other: OECD 421
Species:
Sex:
Strain:
Route of admin.:
Exposure period:
5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : 
Strain : 
Route of admin. : other: not specified
Exposure period : 
Frequency of treatm. : 
Duration of test : 
Doses : 
Control group : 

Result : Triethyl phosphite induced polymorphic defects, but especially cleft palate and agnathia, in the rat (Mehlman, 1984)

Reliability : (3) invalid secondary literature, primary source (Mehlman Toxicol.Appl.Pharmacol. 72, 1119-123 (1984)) does not contain data on triethyl phosphite

28.01.2003

Species : other: OECD 421
Sex : 
Strain : 
Route of admin. : 
Exposure period : 
Frequency of treatm. : 
Duration of test : 
Doses : 
Control group : 

Remark : Developmental toxicity was assessed in a study according to OECD TG 421.
This study is described under:
Chapter 5.8.3; Toxicity to reproduction, other studies

07.02.2003
5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

<table>
<thead>
<tr>
<th>Type</th>
<th>other: OECD 421</th>
</tr>
</thead>
<tbody>
<tr>
<td>In vitro/in vivo</td>
<td>In vivo</td>
</tr>
<tr>
<td>Species</td>
<td>rat</td>
</tr>
<tr>
<td>Sex</td>
<td>male/female</td>
</tr>
<tr>
<td>Strain</td>
<td>Wistar</td>
</tr>
<tr>
<td>Route of admin.</td>
<td>gavage</td>
</tr>
<tr>
<td>Exposure period</td>
<td>2 weeks before mating, during the 2 week mating and 1-week remating period, during gestation, lactation and up to the day before necropsy (males were necropsied on day 36 to 37 of treatment, females between day 4 to 6 post partum)</td>
</tr>
<tr>
<td>Frequency of treatm.</td>
<td>daily</td>
</tr>
<tr>
<td>Duration of test</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Doses</td>
<td>0 -10 - 80 - 320 - 640 mg/kg bw</td>
</tr>
<tr>
<td>Control group</td>
<td>yes, concurrent vehicle</td>
</tr>
<tr>
<td>Method</td>
<td>other: OECD 421 (1995)</td>
</tr>
<tr>
<td>Year</td>
<td>2002</td>
</tr>
<tr>
<td>GLP</td>
<td>yes</td>
</tr>
<tr>
<td>Test substance</td>
<td>other TS: triethyl phosphite, 99.3% active ingredient</td>
</tr>
</tbody>
</table>

**Result**

**MORTALITY:**
- F0: 640 mg/kg: male:1/12 (d 20, not treatment related)
- 640 mg/kg: female:12/12 (d 23-25 =mating or early gestation, moribund)
  - F1: 320 mg/kg: 13/13 (1 day after birth)

**OBSERVATION:**
- F0: salivation (all groups including control, immediately after dosing, dose dependently increased incidence)
- 640 mg/kg: male: tremors(1/11), piloerection(6/11), sunken sides(6/11), skin lesion(1/11)
- 640 mg/kg: female(all): hypoactivity, piloerection, sunken sides, circling behavior, skin lesion, loss of weight, recumbency,
- 320 mg/kg: female(1/12): hypoactivity, piloerection, sunken sides, high stepping gait
  - F1: >= 320 mg/kg bw/day: hypothermia, low birth weight

**BODY WEIGHT GAIN:**
- F0: males and females: 640 mg/kg: transient increase, then severe decrease; overall: no weight gain at all = >14% decrease relative to control in males and females
- slight effects in individuals at 80 (before the increase of weight due to gestation) and 320 mg/kg bw
  - F1: <= 80 mg/kg: no effect

**FOOD CONSUMPTION:**
- males: no effect
- females: possibly slight reduction during lactation at 80 mg/kg bw (highest dose at that time; no surviving pups at 320 mg/kg bw)

**WATER CONSUMPTION:**
- males + females: no effect
NECROPSY: 640 mg/kg: female: small spleen in moribund rats

ORGAN WEIGHTS:
testes: 640 mg/kg: abs: slight decrease (Control: 1.637g, treated: 1.321g)
rel: slight increase (Control: 0.868%, treated: 0.981%)
Relative testes weights (%) were 0.87, 0.89, 0.91, 0.85, 0.98** for controls, 10, 80, 320 and 640 mg/kg bw/day groups, respectively; there was no significant difference in absolute testes weights between the groups.

HISTOPATHOLOGY:
(reproductive organs + macroscopically altered tissues)
males: 640 mg/kg: testes: min.-slight cell degeneration
females: 640 mg/kg:
mammary gland: slight proliferation/secretion, vagina+cervix: mucification
spleen: reduced lymphoid cellularity (perimortal)
males+females: <=320 mg/kg: no treatment related effects

TIME TO INSEMINATION:
increase at 320 mg/kg

INSEMINATION INDEX:
0 - 320 mg/kg: 100%
640 mg/kg: 41.7%

FERTILITY INDEX:
0 mg/kg: 60%;
10 mg/kg: 75%;
80 mg/kg: 100%;
320 mg/kg: 58.3%
640 mg/kg: no surviving dam

DURATION OF GESTATION:
reduction at 320 mg/kg

GESTATION INDEX:
0 mg/kg: 100%;
10 mg/kg: 100%;
80 mg/kg: 100%;
320 mg/kg: 28.6%
640 mg/kg: no surviving dam

NUMBER OF CORPORA LUTEA, NUMBER OF IMPLANTATIONS: no effects

LITTER SIZE: no effect

SEX RATIO OF PUPS: 320 mg/kg: reduction of males (equivocal due to small number of pups)

FETAL DEVELOPMENT:
In F1 developmental parameters were not affected by treatment up to and including doses of 80 mg/kg bw/day, while evaluation was not possible at higher doses as there were no surviving pups. No externally malformed pups were observed.

NOEL(males): 320 mg/kg bw (salivation already at 10 mg/kg bw)
NOEL(females): 10 mg/kg bw (due to weight loss and reduced food consumption at 80 mg/kg and above)
NOEL(reproduction): 80 mg/kg bw
Test condition : ANIMALS: SPF bred Wistar rats (Hsd Cpb:WU), between 318 and 353 g (m), and 192-214 g (f), age: 11 weeks (m), 12 weeks (f) 
(12m + 12 f)/treatment group 
(15m + 15 f)/control group 

VEHICLE: polyethylenglycol 400 

MATING: overnight, 1:1, daily during the 2-week mating period. 

PARAMETERS: 
mortality, observation, body weight, food consumption, water consumption, 
necropsy, histopathology (testes, epididymides, ovaries, mammae, uterus, 
vagina and organs with+ macroscopically altered tissues), time to 
insemination, insemination index, fertility index; duration of gestation, 
gestation index, number of corpora lutea, number of implantations 

F1 pups: appearance (including externally visible malformations), general 
beholder, mortality, sex ratio at birth, individual weights at birth and on day 
4 after birth 

STATISTICAL METHODS: ANOVA, chi-square, Fisher’s exact test, F-test 
and additional t-test or Welch-t-test, significance levels p=0.05 and 0.01 

Reliability : (1) valid without restriction 

Flag : Critical study for SIDS endpoint 

5.10 EXPOSURE EXPERIENCE 

5.11 ADDITIONAL REMARKS 

Type : Neurotoxicity 

Remark : hen, oral: single administration, observation period 6 
weeks, 0.1 and 0.5 ml/kg bw: no clinical signs of 
neurotoxicity, no paralysis 

Reliability : (4) not assignable 
Insufficient detail reported to assess reliability 

20.01.2003
OECD SIDS

TRIETHYL PHOSPHITE

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ID: 122-52-1

DATE: 12.01.2005

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