



Human & Environmental Risk Assessment on
ingredients of
European household cleaning products

Sodium Tripolyphosphate (STPP)
CAS: 7758-29-4

DRAFT

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2 *Executive Summary*

Sodium tripolyphosphate (STPP) is a solid inorganic compound used in a large variety of household cleaning products, mainly as a builder, but also in human foodstuffs, animal feeds, industrial cleaning processes and ceramics manufacture.

STPP is widely used in regular and compact laundry detergents (powder, liquid, gel, tablets), automatic dishwashing detergents (powder, liquid, gel, tablets), toilet cleaners, and surface cleaners, and provides a number of functions including sequestration of “water hardness” enabling surfactants to function effectively, pH buffering, dirt emulsification and prevention of deposition, hydrolysis of grease, and dissolving-dispersing dirt particles. In the year 2000, the total consumption of STPP in these applications was estimated to be approximately 300 000 tonnes in Western Europe and this is estimated to represent 90-95% of STPP use in Europe.

Environmental risk assessment

Due to its physico-chemical properties, STPP is not distributed or transported to the atmosphere, and thus is not expected to end up in soil *via* atmospheric deposition. Because it is very water-soluble, it is not significantly transferred to sewage sludge, and therefore to soil by sludge spreading. No environmental risk related to STPP use in detergents is indicated in soil or air.

As an ingredient of household cleaning products, STPP present in domestic waste waters is mainly discharged to the aquatic compartment, directly, *via* waste water treatment plants, *via* septic tanks, infiltration or other autonomous waste water systems.

As STPP is an inorganic substance, biodegradation studies are not applicable. However, STPP can be hydrolysed, finally to orthophosphate, which can be assimilated by algae and/or by micro-organisms. STPP thus ends up being assimilated into the natural phosphorus cycle.

Reliable published studies confirm biochemical understanding, showing that STPP is progressively hydrolysed by biochemical activity in contact with waste waters (in sewerage pipes and within sewage works) and also in the natural aquatic environment.

This information enabled the calculation of “worst case” PEC (Predicted Environmental Concentrations) using the EUSES model and the HERA detergent scenario. A default regional release of 10 % was applied instead of the 7 % regional release indicated in the HERA detergent scenario.

Reliable acute aquatic ecotoxicity studies are available which show that STPP is not toxic to aquatic organisms: all EC/LC50 are above 100 mg/l (daphnia, fish, algae). Because of this, and because of the only temporary presence of STPP in the aquatic environment (due to hydrolysis), no studies have been carried out to date concerning the chronic effects of STPP on these aquatic organisms. PNEC (Predicted No Effect Concentrations) were therefore calculated for the aquatic environment and sediments on the basis of the acute aquatic ecotoxicity results.

PEC/PNEC ratio >1 were obtained for STPP in the local water and sediment compartments (2.5 and 3.18 respectively). STPP has been used for many years. It is an authorised food and drug additive. It did not show any acute toxicity effect to the aquatic organisms tested. It is anticipated that the PEC/PNEC ratios >1 obtained for the local water and sediment scenarios are the consequence of the use of the 1,000 Assessment Factor in the calculation.

To refine the aquatic PNEC of STPP, CEEP (Centre Européen d'Etudes des Polyphosphates) has planned acute toxicity tests on *Daphnia magna* and *Ceriodaphnia dubia*, as well as a chronic toxicity test on the most sensitive species if necessary.

Concerning the possible environmental impact of STPP-based orthophosphate (PO_4^{3-}), a preliminary risk characterisation based on simplified but conservative assumptions was conducted. A PEC/PNEC ratio < 1 was obtained for the local water compartment, indicating that orthophosphate resulting from the hydrolysis of STPP does not present a risk for the aquatic environment.

The eutrophication of surface waters due to nutrient enrichment is not addressed in this document because a PNEC cannot be defined for such effects, which depend on many factors varying spatially and temporally (temperature, light, concentrations of phosphates and of other nutrients, activity of grazer population ...).

Human Health risk assessment

Consumers can be exposed to STPP from household cleaning products by all routes, skin contact, oral ingestion, or by inhalation. Using scenarios relevant to consumer uses, the total potential exposure was estimated to be 33 $\mu\text{g}/\text{kg}/\text{day}$.

The toxicological database shows that STPP has a low acute toxicity by ingestion and dermal application. At the maximum attainable concentration of STPP that could be technically generated, no significant clinical signs were observed except reactions consistent with exposure to an irritant dust.

STPP was not found irritating to the intact skin or to the eyes when tested neat or in aqueous solutions. Experimental data that were available with detergent formulations containing STPP showed no skin contact sensitisation potential under typical use conditions. Furthermore, there are also no reports of skin sensitisation occurrence associated with STPP exposure in consumers.

Based on literature data, STPP is not considered to be mutagenic or genotoxic. The oral long-term toxicity study did not show any evidence of a carcinogenic potential of STPP in a chronic study in rats. There was no evidence of adverse reproductive or developmental effects in various species at the doses tested.

No repeated dose toxicity studies were available in animals for the dermal route, or by inhalation. However, repeated dose toxicity studies in rats by the oral route showed that STPP at high doses induced retarded growth, anaemia and renal calcification. In a 2-year study, no toxic effect was observed at the doses of up to 0.5%, which was used to estimate a systemic NOEL of 225 $\text{mg}/\text{kg}/\text{day}$. The effects induced by STPP were similar to those reported for other condensed inorganic phosphates.

As Phosphorus accounts for 25.3% of the STPP molecule, the total intake of Phosphorus through the use of STPP in detergents (8.4 µg P/kg/day) is minor when compared to the estimated typical dietary intake of Phosphorus in European countries (ca. 24 mg/kg/day) and to the Maximum Tolerable Daily intake established for total Phosphorus intake from all dietary sources (70 mg/kg/day).

Comparison of the total combined estimated systemic consumer exposure to STPP with the systemic NOEL results in a margin of exposure of 6 800 that can be considered large enough to conclude that STPP is of low concern for consumer use in household detergents, taking into account inherent uncertainties, variability of the database and extrapolations.

3 Substance Characterisation

3.1 CAS No and Grouping Information

The general term "condensed inorganic phosphates" is applied to phosphorus compounds in which various numbers of PO₄ groups are linked together by oxygen bridges. They fall into three classes : cyclic, linear and cross-linked condensed phosphates.

In condensed inorganic phosphates, phosphorus is at the highest oxidation state (+5).

Linear condensed phosphates, also called polyphosphates have the general elementary composition : [P_nO_{3n+1}]⁽ⁿ⁺²⁾⁻ (cf. Table 1).

Table 1. Phosphates

Number of P Atoms	Type	Example	CAS n°
1	monophosphates/ orthophosphates	Na ₃ PO ₄	7601-54-9
		Na ₂ HPO ₄	7558-79-4
		NaH ₂ PO ₄	7558-80-7
2	biphosphates/ pyrophosphates	Na ₄ P ₂ O ₇	7722-88-5
		Na ₃ HP ₂ O ₇	14691-80-6
		Na ₂ H ₂ P ₂ O ₇	7758-16-9
		NaH ₃ P ₂ O ₇	13847-74-0
3	triphosphates	Na ₅ P ₃ O ₁₀	7758-29-4
		Na ₄ HP ₃ O ₁₀	24616-37-3
		Na ₃ H ₂ P ₃ O ₁₀	-
4	tetraphosphates	...	
		Na ₆ P ₄ O ₁₃	-
...		...	

Analogous compounds are known with other metallic counter ions (calcium for example), and mixed salts exist (calcium and sodium mixed salts for example)

Phosphate chemistry is complex, and in the environment many species may exist depending on the conditions (hardness, pH, ...)

The present HERA risk assessment addresses sodium tripolyphosphate Na₅P₃O₁₀ (STPP) with CAS-No 7758-29-4 (pentasodium triphosphate, or Triphosphoric acid, pentasodium salt; EINECS No. 231-838-7) which is the form in which "phosphates" are widely used in detergents and cleaning products. However, in some cases, data on sodium triphosphate Na_xO₁₀P₃ with CAS-No 13573-18-7 (Triphosphoric acid, sodium salt, EINECS No. 237-004-9) were used.

3.2 Chemical structure and Composition

Sodium tripolyphosphate is a solid, inorganic compound present in the form of slightly hygroscopic granules. The stable form of STPP is the hexahydrated salt.

The anhydrous salt exists in two crystalline forms called Phase 1 and Phase 2. The amount of each phase in a product depends on the calcination temperature in the production process. Bulk densities range from 0.45 to 1.15 g/cm³. Depending on the use of STPP, products of different bulk densities, percentage of hydrated forms, percentage of Phase 1/Phase 2 forms, are commercialised.

Impurities of sodium tripolyphosphate may include sodium pyrophosphate, sodium orthophosphate and sodium metaphosphate. Typical analysis give :

STPP	96 %
Pyro + Ortho + Metaphosphate	4 %

The impurity profile depends of the production process and the composition of the raw materials.

Anhydrous STPP does not melt, but decomposes into pyrophosphate around 620°C (Pascal, 1956). The hexahydrated form decomposes at 85 °C (Pascal, 1956).

The relevant physico-chemical properties of STPP are summarised in Table2.

Table 2. Identity and physical/chemical properties of sodium tripolyphosphate.

CAS N° :7758-29-4 EINECS : 231-838-7	PROTOCOL	RESULTS/REMARKS	REF.
Macro-molecular description (Physical State/Particle size)		solid, inorganic slightly hygroscopic granules	
Molecular Weight	calculated	367.86 [g/mol]	
Melting Point	Other*	decomposes at 620°C	1
Boiling Point		not applicable	
Vapour Pressure at 25°C		negligible	
Octanol-water Partition Coefficient (Log Pow)		not applicable	
Water Solubility	Other*	at 20°C 140 [g/kg] at 25°C 145 [g/l] at 40°C 160 [g/kg] at 100°C 325 [g/l]	2,3
Sorption coefficients		not available	
Koc		not available	
Density	Bulk density	0.45-1.15 [g/cm ³] at ambient temp.	4
Viscosity		not applicable	
pH-Value	Other*	at 25 °C : 9.0-10 in 1% aqueous solution	2
pKa	Other*	H ₅ P ₃ O ₁₀ ↔ H ⁺ + H ₄ P ₃ O ₁₀ ⁻ (pK1 = -∞) H ₄ P ₃ O ₁₀ ⁻ ↔ H ⁺ + H ₃ P ₃ O ₁₀ ²⁻ (pK2 = 1.1) H ₃ P ₃ O ₁₀ ²⁻ ↔ H ⁺ + H ₂ P ₃ O ₁₀ ³⁻ (pK3 = 2.3) H ₂ P ₃ O ₁₀ ³⁻ ↔ H ⁺ + HP ₃ O ₁₀ ⁴⁻ (pK4 = 6.3) HP ₃ O ₁₀ ⁴⁻ ↔ H ⁺ + P ₃ O ₁₀ ⁵⁻ (pK5 = 8.9)	5
Henry's constant		negligible	

1 Pascal (1956)

2 Rhodia internal data

3 Weast (1979)

4 Rhodia Product Data Sheets

5 *Beukenkamp et al. (1954), Watters et al. (1956), Watters et al. (1957), Wolhoff and Overbeek (1959)*

**Method not contained in the IUCLID glossary of standard methods*

3.3 Manufacturing Route and Production/Volume Statistics

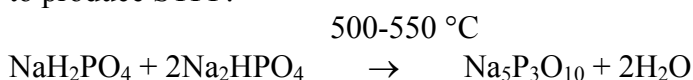
Sodium tripolyphosphate is produced from phosphate rock. Two STPP manufacturing routes are currently used : the thermal route and the wet route.

The thermal route uses high temperature reducing conditions and produces phosphorus vapour from phosphate rocks. The phosphorus is then burnt in air to form phosphoric acid. No STPP for detergent applications is produced by the thermal route.

In the wet process, phosphoric acid is produced by “attacking” phosphate rock with sulphuric acid.

Most imports to Western Europe are in the form of crude phosphoric acid. Phosphoric acid is further purified to prepare high purity phosphoric acid.

STPP is prepared from purified phosphoric acid by neutralisation with sodium hydroxide forming sodium hydrogen phosphates. Sodium hydrogen phosphates are heated to 500-550 °C to produce STPP.



The amount of STPP which was used in household cleaning products in Europe in 2000, is estimated to be about 300 000 tonnes (communication from AISE). STPP consumption in household detergents varies considerably between different countries in Europe.

It should be pointed out that in some countries the STPP use in detergents is almost exclusively concentrated on automatic dishwashing products while in other countries the use in laundry detergents is the overwhelming application.

3.4 Use Applications

In household cleaning products, sodium tripolyphosphate is used most widely as builder. In conjunction with surfactants, it allows detergents to perform efficiently in all washing conditions. It is widely used in laundry detergents, dishwasher detergents, industrial and institutional detergents. Household cleaning applications are estimated by industry to account for 90-95% of STPP use in Europe.

STPP fulfils several important functions in detergents:

- inhibits the effects of calcium and magnesium salts present in hard water and in soils by sequestering these ions.
- re-dissolves calcium and magnesium compounds present in the washing machine from previous washes.
- prevents the deposit of calcium and magnesium incrustations on the washing machine’s heating elements.

- avoids re-deposition of dirt and incrustations on fabrics
- stabilises alkalinity at the correct level throughout the washing process.
- helps break up large particles of dirt into smaller ones, which can be washed out.
- hydrolyses grease and oils, facilitating their removal in the washing process
- helps the efficient manufacture, storage and use of detergents by stabilising their physical properties.
- facilitates dissolving of detergents.

The STPP content of P-containing household cleaning products is given in the human health assessment part in § 5.1.1 (Consumer exposure/Product types).

In addition, STPP has other uses as : industrial cleaning processes, food additive (food processing, baking, food additive ...), animal feeds and ceramics manufacture. These uses are relatively minor compared to household and are outside the scope of HERA and therefore will not be considered in this risk assessment.

4 Environmental Assessment

4.1 Environmental Exposure Assessment

4.1.1 Environmental fate

Due to its physico-chemical properties, STPP is not distributed or transported to the atmosphere. Thus, the environmental risk assessment will not focus on this compartment.

As an ingredient of household cleaning products, STPP present in domestic waste waters is mainly discharged to the aquatic compartment, directly, *via* waste water treatment plants, *via* septic tanks, infiltration or other autonomous waste water systems.

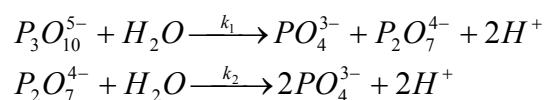
As STPP is an inorganic substance, biodegradation studies are not applicable. However, STPP can be hydrolysed in water to pyrophosphate and then to orthophosphate which can be assimilated by algae and/or by micro-organisms. STPP thus ends up in products which may be assimilated into the natural phosphorus cycle.

Although STPP main degradation product is orthophosphate, the environmental risk assessment will focus on STPP.

4.1.1.1 Abiotic/biotic degradation

Hydrolysis in Sterile Media

The hydrolysis of sodium tripolyphosphate was investigated in sterile aqueous buffers at pH 3, 4, 5 and 7, and at temperatures between 40 and 70 °C, by Zidner, Hertz and Oswald (1984). The experimental data were in good agreement with the following mechanism and gave a pseudo first-order reaction law.



In sterile water the predicted half-life of tripolyphosphate at pH 7-8 and at 20 °C is in the order of years.

The kinetics of hydrolysis of tripolyphosphate and pyrophosphate were also studied in sterile lake water and sterile algal culture media by Clesceri and Lee (1965a), and compared to published results obtained in distilled water.

Both compounds hydrolysed 100-1000 times quicker in sterile lake water than in distilled water, and about 5-10 times slower in sterile algal media than in sterile lake water. The increase of the hydrolysis rates was attributed to dissolved substances such as calcium. In sterile medium triphosphate hydrolysed slightly quicker than pyrophosphate. STPP half-lives in sterile lake water and algal medium ranged between 83 h and 608 h at 23°C.

Hydrolysis in surface water

The rates of hydrolysis of tripolyphosphate and pyrophosphate in non-sterile media at 25 °C were also determined by Clesceri and Lee (1965b). The media utilised were lake water supplemented or not with glucose. Initial triphosphate and pyrophosphate concentrations were 0.5 mg P/l.

The results showed that tripolyphosphate and pyrophosphate were hydrolysed in orthophosphate in a period of several days. Addition of glucose increased the rate of hydrolysis, indicating that microbial activity was one of the primary mechanisms of hydrolysis.

In non-sterile medium pyrophosphate hydrolysed slightly quicker than triphosphate.

From these data an hydrolysis rate constant in natural surface water has been calculated at 25 °C for STPP by linear regression analysis of the logarithm of the concentrations *versus* time :

$$k_{\text{STPP/water/25}^{\circ}\text{C}} = 0.2369 \text{ d}^{-1}$$

$$\text{DT}_{50\text{STPP/water/25}^{\circ}\text{C}} = 70.2 \text{ h}$$

$$\text{Correlation coefficient} = -0.949062$$

An hydrolysis rate constant at 12 °C (default average value for European surface waters) can be extrapolated using the Arrhenius law :

$$k_{\text{STPP/water/12}^{\circ}\text{C}} = 0.0837 \text{ d}^{-1}$$

$$\text{DT}_{50\text{STPP/water/12}^{\circ}\text{C}} = 198.7 \text{ h}$$

This rate constant of 0.0837 d⁻¹ has been used in the EUSES model (see § 4.1.4 PEC calculations) to estimate the hydrolysis rate constant in surface water.

Comparable results were also obtained by Engelbrecht and Morgan (1959) in various river water samples (reported half-lives at 29°C ranged from 9.6 h to 768 h depending on the sampling locations), and by Shannon and Lee (1966) in lake and river waters (half-lives derived from reported rates of hydrolysis at 20°C ranged from 193.4 h to 414.3 h).

Hydrolysis in sewage

Davis and Wilcomb (1967) studied the rate of hydrolysis of condensed phosphates STPP and TKPP (tetrapotassium pyrophosphate) in a raw domestic sewage from a municipal treatment plant at 28 °C. Rapid rates of hydrolysis were observed in the first 48 hours. 80 % and 86 % of all the condensed forms present (condensed phosphate originally present in the sewage plus STPP or TKPP respectively) were hydrolysed in the first 48 hours, while only 35.6 % of the condensed forms in the control, with no STPP or TKPP added, were hydrolysed in the same length of time.

Finstein and Hunter (1967) showed that around 50% of incoming detergent polyphosphate were hydrolysed in the aerobic compartments of different examined sewage works, and a similar proportion in a trickling filter unit.

Halliwell et al. (2001) detected detergent condensed phosphates in raw sewage entering a small, predominantly domestic waste water treatment facility located in a small rural township, indicating that triphosphate did not undergo complete hydrolysis during the dish or clothes washing, or transport through the sewerage to the sewage treatment plant. The total

transit time of sewage discharged from a household until it reached the treatment facility was estimated to be 2.6 hours. In contrast, Jolley (1993) found complete hydrolysis of triphosphate by the time the effluent reached the sewage treatment plant in a large urban area.

Halliwell et al. (2001) also studied the hydrolysis of STPP in the raw sewage entering the WWTP of this small rural township treating exclusively domestic sewage. Triphosphate was spiked to give an initial concentration of 2 mg P/l.

The degradation of triphosphate exhibited pseudo-first-order reaction kinetics with the following rate constants :

$$k_{\text{TPP/sewage}/15^{\circ}\text{C}} = 2.59 \times 10^{-5} \text{ s}^{-1} = 0.093 \text{ h}^{-1}$$

$$k_{\text{TPP/sewage}/20^{\circ}\text{C}} = 6.47 \times 10^{-5} \text{ s}^{-1} = 0.233 \text{ h}^{-1}$$

corresponding to half-lives of 7.42 h and 2.97 h at 15 °C and 20 °C respectively.

This degradation rate constant of 0.093 h⁻¹ at 15°C has been used to evaluate the percent STPP degradation in the generic WWTP of the EUSES model (see § 4.1.2 Removal, § Removal in the sewerage and in the WWTP).

4.1.1.2 Bio-assimilation

STPP is hydrolysed in the sewerage pipes, the sewage treatment plants and the environment to orthophosphate which is then bio-assimilated by the bacterial populations and the aquatic plants and algae found in these different compartments.

Bio-assimilation of phosphorus in sewage treatment plants was studied and is reported by A. Hamm (1989). An average P elimination of 40% was found in mechanical-biological processes. Part of this elimination is due to bio-assimilation by the sewage sludge. The same value is reported in the WRC report for the EU Environment Directorate (Glennie E.B. *et al*, 2002).

Hydrolysis and assimilation of triphosphate, pyrophosphate and orthophosphate were determined by Clesceri and Lee (1965b) in *Chlorella pyrenoidosa* cultures : in non-sterile culture and in sterile culture (bacteria free). Cultures were incubated at 23 °C. Initial concentrations were 0.5 mg P/l.

The study showed that a faster rate of hydrolysis occurred with non-sterile rather than sterile cultures of *Chlorella pyrenoidosa*. In non-sterile cultures, no condensed phosphate was left in the media after 75 h of incubation. The presence of non-algal micro-organisms such as bacteria increased the rate of hydrolysis of the two condensed phosphates.

Non-sterile and sterile cultures of *Chlorella* grew best (expressed as growth rates and final biomass) when the phosphorus source was orthophosphate.

The rates of hydrolysis and assimilation of STPP and TKPP (tetrapotassium pyrophosphate) by pure cultures of green algae were studied by Davis and Wilcomb (1967) in static and flow-through systems with six different species of algae. Pure cultures of green algae species demonstrated some hydrolytic activity and varying abilities to assimilate phosphorus depending on the conditions of experimentation. The different algae species preferred orthophosphate to condensed phosphate when both molecules were present in the medium. A

greater hydrolytic/assimilation activity was observed in flow-through system than in static ones.

The ability of triphosphate to hydrolyse to orthophosphate and therefore to be assimilated by aquatic plants and algae may lead in certain circumstances to eutrophication phenomena in the aquatic environment. This point is discussed in § 4.5 Eutrophication.

4.1.1.3 Complexation of metals by STPP

Sodium tripolyphosphate is able to form with metals (Ca, Mg, Fe, ...), anions of complex salts such as:

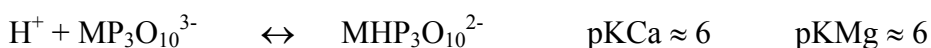


The reaction of STPP with Ca^{++} can be schematised as follows:



$\text{Ca}_5(\text{P}_3\text{O}_{10})_2$ is insoluble and precipitates.

Numerous studies were carried out to determine the constants of equilibrium (Martell and Schwarzenbach, 1956; Watters and Lambert, 1958; Wolhoff and Overbeek, 1959; Ellison and Martell, 1964; Miura and Moriguchi, 1964; Anderegg, 1965; Hollingsworth, 1978). Precise determination is difficult due to the complexity of the media, which explains the variability of the results (Isnard, 1991) :



This property of phosphates (including triphosphate) to precipitate in presence of metal ions is used in Waste Water Treatment Plants where phosphates are eliminated by chemical precipitation with ferric or aluminium salts.

Thus complexation of triphosphate to insoluble metal complex species is expected to contribute to the transformation of STPP and to its partitioning from the water column in the sewerage pipes, the sewage treatment systems and the aquatic environment.

After reaction with metal ions, the insoluble species formed will settle onto the sediments. These insoluble species are expected to only be slowly accessible to hydrolysis, and re-mobilisation of triphosphate and metal ions is not expected.

4.1.1.4 Adsorption/Desorption

Tripolyphosphate and its soluble complex salts are not expected to adsorb highly onto the solid particles of the aquatic environment, due to their solubility.

4.1.1.5 Fate in soils

In soils, it is expected that STPP is also hydrolysed and bio-assimilated via the same mechanisms as in the aquatic environment.

Formation of complex insoluble species most probably occurs in soils. Thus, it is expected that STPP may also be transformed in soils to insoluble forms which remain trapped in soils.

4.1.2 Removal

Due to its rapid hydrolysis under conditions relevant in practice, triphosphate is transformed into other soluble forms of phosphorus, mainly orthophosphate. In addition, depending on the presence of cationic ions, triphosphate can precipitate in the form of insoluble calcium, magnesium or other metal triphosphate (see 4.1.1.3). Thus low level of discharges in the form of STPP is expected.

Removal in the washing machines :

STPP hydrolysis starts in the washing machine. Analysis performed at the outlet of laundry washing machines showed that at least 20 % of STPP were hydrolysed (Galliot, 1985).

Halliwell et al. (2001) investigated the stability of STPP in washing machines and in dishwashers. The washing machine experiments were conducted with detergents with a low (1.48 % P w/w) and high (8.17 % P w/w) phosphate content using both hot and cold water cycles. The dishwashing experiment was conducted on one detergent (9.5 % P w/w). STPP degradations ranged from 0 % for high P content and low temperature, to 28 % for low P content and high temperature, and 33 % for low P content and low temperature.

These studies show that 0% to 30% of STPP may be hydrolysed in the washing process.

Removal in the sewerage and in the WWTP :

STPP removal continues in the sewerage network and in the waste water treatment plant by hydrolysis, bio-assimilation and precipitation.

Davies and Wilcomb (1967) showed that 80 % of triphosphate was hydrolysed in less than 48h in domestic sewage (cf § 4.1.1.1. Abiotic/biotic degradation, § Hydrolysis in sewage).

Halliwell et al. (2001) obtained a degradation rate constant of 0.093 h^{-1} in sewage at $15 \text{ }^{\circ}\text{C}$ (cf § 4.1.1.1. Abiotic/biotic degradation, § Hydrolysis in sewage). This rate constant at 15°C (default EUSES value for the temperature in WWTP) can be used to derive a percentage of degradation in a generic WWTP using the following residence times :

- 2.6 h in the sewerage network (residence time in the sewerage network of a small rural township, considered as a reasonable worst case)
- 2.0 h in the primary settler (default EUSES value)
- 6.9 h in the activated sludge tank (default EUSES value)
- 6.0 h in the solids-liquids separator (default EUSES value)

and applying a pseudo-first-order kinetics, a degradation of 80 % of STPP is obtained.

Thus, it can reasonably be assumed that in the sewerage network and sewage treatment plants 80 % of STPP is removed by hydrolysis, bioassimilation and precipitation. The remaining 20 % is released in water, as STPP is highly soluble and is not expected to adsorb significantly onto sludge.

This figure is considered as conservative, as it does not consider the P-treatment stage required by the EU Urban Waste Water Treatment Directive for WWTPs of > 10 000 eq. inh. in sensitive area. This P-treatment can be achieved by physico-chemical processes, in which case triphosphate is precipitated as the other phosphate salts to insoluble complex salts, or by biological processes where triphosphate is hydrolysed and bio-assimilated. Up to 95% P removal can be achieved with biological and/or chemical precipitation processes (Glennie E.B. *et al.*, 2002).

4.1.3 Monitoring Studies

No monitoring studies are available on STPP.

Numerous monitoring programmes of total phosphorus concentrations in European rivers are available. Main results are presented in the WRC report for the EU Environment Directorate (Glennie E.B. *et al.*, 2002). Highest median total phosphorus concentrations range from 0.2 mg P/l to 1.2 mg P/l.

4.1.4 PEC Calculations

PEC calculations were performed with EUSES software using the HERA detergent scenario except for the regional release fraction value. The percent of continental tonnage released to the region, set up at 7 % in the HERA detergent scenario, has not been used as the STPP usage in the individual European countries is significantly different. Therefore the default TGD 10%-rule for private use has been applied.

The rate constant for hydrolysis in surface water was set up at : 0.0837 d⁻¹ (cf § 4.1.1.1. Abiotic/biotic degradation, § Hydrolysis in surface water).

The main uses of STPP are in laundry detergents and in machine dishwashing detergents. At this stage of the risk assessment, it has been considered that STPP is not transformed during the washing process (cf. § 4.1.2 Removal, § Removal in the washing machines).

In sewage treatment, the fraction of emission directed to water was set up at 0.20, and the fraction of emission degraded at 0.80 (cf. § 4.1.2 Removal, § Removal in the sewerage and in the WWTP). This is a conservative estimate, as it assumes no P-treatment in WWTPs as required in certain conditions by the EU Urban Waste Water Treatment Directive.

Zero removal is assumed in sewerage piping where domestic wastewaters are not discharged *via* sewage works.

No significant quantities of STPP is expected to remain as such in sludge. The Simpletreat model integrated in EUSES software predicted a STPP fraction of emission directed to sludge of $2.44 \cdot 10^{-3}$, and a concentration in dry sewage sludge of 1.91 mg/kg, based on the physico-chemical properties of STPP.

Due to its negligible vapour pressure, no STPP is distributed to air.

Calculated PEC are presented in Tables 3a and 3b.

Table 3a. Local PEC values from EUSES calculations

Local PEC	Value
PEC in surface water (mg/l)	0.694
PEC in sediment (mg/kg wwt)	0.546
PEC for micro-organisms in the STP (mg/l)	6.16
PEC in air (mg/m ³)	0
PEC in agric. soil averaged over 30 d (mg/kg wwt)	$2.4 \cdot 10^{-3}$
PEC in agric. soil averaged over 180 d (mg/kg wwt)	$1.19 \cdot 10^{-3}$
PEC in grassland averaged over 180 d (mg/kg wwt)	$2.63 \cdot 10^{-4}$

Table 3b. Regional PEC values from EUSES calculations

Regional PEC	Value
PEC in surface water (mg/l)	0.0772
PEC in sediment (mg/kg wwt)	0.0466
PEC in air (mg/m ³)	0
PEC in agric. soil (mg/kg wwt)	$1.88 \cdot 10^{-5}$
PEC in natural soil (mg/kg wwt)	0

4.2 Environmental effects assessment

4.2.1 Toxicity

4.2.1.1 Ecotoxicity - Aquatic : Acute Test Results

Table 4 compiles the available data on the acute aquatic toxicity of STPP.

Table 4. Results of Acute Aquatic Ecotoxicity

	Species	Protocol	Endpoint	Result (mg/l)	Reliability acc. to Klimisch	Reference
Invertebrate	<i>Daphnia magna</i>	CFR 40, Subpart B, 7971300	IC50, 48h	>100	1	Vaishnav et al., (1991)
	<i>Daphnia magna</i>	AFNOR T90 301	IC50, 24h	1150	1	Dion, (1985)
	<i>Ceriodaphnia cf. dubia</i>	Other*	EC50, 48h	277	1	Warne et al., (1999)
	Daphnia	Other*	LC0, 24h	1000	4	Kastner et al., (1983)
Fish	Zebra fish	AFNOR T90 303	LC50, 24h	1850	1	Dion, (1985)
	Trout	Other*	LC0, 48h	500	4	Kastner et al., (1983)
Algae	<i>Scenedesmus subspicatus</i>	ISO/DP 8692	ErC50, 4 d	160	3	Herschke et al., (1985)
	<i>Skeletonema costatum</i>	AFNOR T95E doc.50F	EbC50, 6 d	>900	3	Herschke et al., (1985)
Micro-organisms	Activated sludge	OECD 209	EC50, 3 h	>1000	4	Hoechst, (1989), cited in IUCLID

* Method not contained in the IUCLID glossary of standard method

Effects on invertebrates

An acute toxicity test with *Daphnia magna* was performed by Vaishnav et al. (1991) under GLP and according to US standard method. No significant immobilisation was observed after 48 hours of exposure to 100 mg/l of sodium tripolyphosphate expressed as nominal concentration. In a range finding study, 1000 mg/l was also found not acutely toxic to the test organisms. The study was considered as reliable without restriction.

An acute toxicity test with *Daphnia magna* was carried out by Dion (1985), in accordance with national standard methods (AFNOR T 90 301). The percentage of immobilisation due to the exposure to sodium tripolyphosphate during 24 hours was reported as follows : IC50 = 1150 mg/l expressed as nominal concentration. The study was considered as reliable without restriction.

Another study, using the cladoceran *Ceriodaphnia cf. dubia* was published by Warne et al. (1999). This study, in accordance with Australian standard methods, showed that the EC50 value after 48 hr exposure to sodium tripolyphosphate was 277 mg/l expressed as nominal concentration. The study was considered as reliable without restriction.

The toxicity of sodium tripolyphosphate to *Daphnia* was also studied by Kastner and Gode (1983). The LC0 after 24 hr exposure was found to be 1000 mg/l, expressed as nominal concentration. But this study is not described in sufficient details. There is no data about test conditions and test organisms. Only one concentration with no observable effect was reported. The study was considered as not assignable.

Effects on fish

A toxicity test with zebra fish exposed to sodium tripolyphosphate was performed by Dion (1985). The percentage of mortality was measured after 24 hours of exposure. The LC50 was 1850 mg/l expressed as nominal concentration. The study was in accordance with national standard methods (AFNOR T 90 303) and considered as reliable without restriction.

The acute toxicity of sodium tripolyphosphate to trout (species not specified) was reported by Kastner and Gode (1983). The LC0 after 48 hours exposure was found to be 500 mg/l, expressed as nominal concentration. But there was no information on the test water chemistry, the test conditions, neither on biological observations. Only one concentration with no observable effect on mortality was reported. The study was considered as not assignable.

Effects on algae

A study with the marine species *Skeletonema costatum* was carried out by Herschke and Cellier, (1983). From 10 mg/l to 320 mg/l of sodium tripolyphosphate and after an exposure time of 6 days, the product stimulated the growth by comparison with the controls, whereas at 900 mg/l it was slightly inhibitory. No analysis of the substance into the test medium was performed. The algae growth was very low in the controls (less than a factor 16 in 144 hours) and the addition of sodium tripolyphosphate at 10 and 32 mg/l led to a steady increase of the algae growth indicating that the test medium is deficient in phosphates. With 100 mg/l and 320 mg/l the growth decreased regularly but at the end of the test it was still higher than in the controls. It is suspected that the positive effect on the algae growth due to the o-phosphate formed by hydrolysis of sodium tripolyphosphate was counterbalanced by the complexation

of metals like Mg^{++} , Cu^{++} , Zn^{++} , B^{3+} ... which are essential to the algae growth. Due to the low growth of controls and the opposite direct and indirect effect of sodium tripolyphosphate on the algae medium, this study cannot be used for derivation of a PNEC in the risk assessment.

The toxicity of sodium tripolyphosphate to *Scenedesmus subspicatus* was assessed by the same authors (Herschke and Cellier, 1983). The EC50 after 90 hours of exposure was found to be 160 mg/l and 69.2 mg/l, for the growth rate and the biomass respectively. The criteria of validity for the growth rate, set out in the OECD Draft Guideline 202 (July 2001), were fulfilled: the coefficient of variation for the daily growth rates in the controls was less than 35% and the coefficient of variation for the average growth in replicate controls was less than 15%. Therefore only the EC50 based on the growth rate is considered. No analysis of the substance into the test medium was performed. The study was in accordance with international standard methods (ISO/TC 147/SC 5/WG 5N 84). Nevertheless on the basis of the observations made for the test on the marine species *Skeletonema costatum* (see above) and since the fresh water medium is clearly less concentrated in metals (K^+ , Na^+ , Mg^{2+} , B^{3+} , Cu^{2+} , Zn^{2+} , Ca^{2+} , Fe^{2+} ) than the marine medium, it is suspected that the algae growth inhibition observed at 32 mg/l and above was probably due to complexing effects between the sodium tripolyphosphate and some essential elements of the medium (cf. 4.1.1.3). This nutrient deficiency may happen on a laboratory scale but will not be relevant in the environment. So this result cannot be used for the PNEC calculation.

Such nutrient depleting effects which may have no relevance in the real environment have been shown for a number of complexing agents like tetrasodium ethylenediaminetetraacetate (Na_4EDTA), phosphonates and NTA. Hence for instance, the Competent Authorities decided not to take into account the results obtained on algae for the classification and for the PNEC calculation of Na_4EDTA . Accordingly, the results obtained from the algal toxicity test of STPP will not be used for the PNEC derivation.

Effects on other species

The toxicity of different phosphates to the freshwater gastropod, *Helisoma duryi*, was studied by Bernhardt et al. (1985). The mortality of neonates and sublethal effects (see chap. 4.2.1.2) were reported for 3 nominal concentrations of phosphates (15, 150 and 1500 mg/l) and an exposure period of 4 weeks. 100% mortality of the neonates was obtained with 1500 mg/l after 7 days of exposure to pentasodium tripolyphosphate and tetrasodium pyrophosphate, and after 21 days of exposure to sodium orthophosphate. As a dose-response relationship was not observed for sodium orthophosphate, this study was considered as not reliable.

In vitro study was performed about the cytotoxicity to fathead minnow fish cells (Brandao et al., 1992). The toxicity test on fish cells was not used for the risk assessment because in vivo fish data are available and they are considered as more reliable than in vitro data. This in vitro study was considered as an unsuitable test system for PNEC derivation.

4.2.1.2 Ecotoxicity – Aquatic: Chronic Test Results

The results of the acute aquatic ecotoxicity showed that sodium tripolyphosphate is not pronouncedly toxic to the aquatic organisms tested, daphnia, fish and algae. Because of this fact, and because of the only temporary presence of STPP in the aquatic environment (due to

hydrolysis), no studies have been carried out concerning the chronic effects of STPP on these organisms.

The chronic toxicity of different phosphates (pentasodium tripolyphosphate, tetrasodium pyrophosphate and sodium orthophosphate) to the freshwater gastropod, *Helisoma duryi*, was studied by Bernhardt et al., (1985). Sublethal effects such as the inhibition of the shell growth after an exposure period of 4 weeks to different nominal concentrations of phosphates (15, 150 and 1500 mg/l) were reported in addition to the observation of the mortality of neonates (see &4.2.1.1, *Effects on other species*). In addition the effects of phosphates on the embryonic development of eggs were evaluated by exposing egg masses during the same period of 4 weeks. Concerning the shell growth, all phosphates showed inhibitory effects with 150 mg/l and significant effects appeared with 15 mg/l for pentasodium tripolyphosphate and tetrasodium pyrophosphate. Nevertheless there was no quality criteria for the controls, and a dose-response relationship was not always observed (no significant difference between 15 mg/l and 150 mg/l for STPP and at 1500 mg/l all the neonates were dead). Moreover such results presumably based on the complexing effects of STPP obtained in tests at a laboratory scale are not relevant for what may happen in the environment. They are thus considered as unsuitable.

Concerning the fertilized egg masses, they were observed daily and no obvious developmental abnormalities or delay in the time of hatching relative to controls were reported for eggs exposed to 15 and 150 mg/l of phosphates. With the concentration of 1500 mg/l, the eggs failed to hatch. The NOEC relative to eggs hatching and embryonic development after an exposure of 4 weeks to STPP is then considered to be 150 mg/l expressed as nominal concentration. Since there was no quality criteria for the controls and the biological observations performed on the embryos were not described, this study was considered as reliable with restrictions.

The inhibitory effects of different phosphates on the shell growth of *Rangia cuneata* (*marine bivalve*) was studied by Bernhardt et al., (1985). The following phosphates, pentasodium tripolyphosphate, tetrasodium pyrophosphate and sodium orthophosphate were tested at 15, 150 and 1500 mg/l nominal concentrations and the rate of radioactive Ca deposition on the shells was measured after a short exposure of 24 hours. Significant differences on calcium deposition were observed for STPP at 15 mg/l and 1500 mg/l. Due to individual variability among animals, a correct dose-effect relationship was not always obtained. An important variability was also observed in the shell growth depending on the period of sampling (organisms were collected at two periods in natural rivers). Moreover as indicated previously, such laboratory studies on the inhibition of the shell growth probably induced by Ca depletion are of little relevance for environmental situations.

4.2.1.3 Terrestrial toxicity

There is no data on acute or chronic toxicity to plants, earthworms or soil micro-organisms.

4.2.1.4 Micro-organisms in Waste Water Treatment Plant (WWTP)

An activated sludge respiration inhibition test was reported by Hoechst (1989) and cited in IUCLID 11/02/2000. This test was performed in accordance with international standards (OECD 209). The EC50 and the EC10 calculated after an exposure time of 3 hours to

pentasodium tripolyphosphate were higher than 1000 mg/l and 500 mg/l respectively. Due to the lack of the original report, this study was considered as not assignable.

4.2.2 Calculation of PNEC

PNEC Water

If available, chronic toxicity results obtained on aquatic and terrestrial organisms are used for the PNEC calculation. Concerning the aquatic compartment, the only reliable chronic data is relative to eggs hatching and embryonic development of *Helisoma duryi* after an exposure period of 4 weeks to STPP and the NOEC is 150 mg/l expressed as nominal concentration. Using this NOEC and an assessment factor of 100, a PNEC of 1.5 mg/l would be obtained. But the sensitivity of *Helisoma duryi* is not known and hence, it cannot be decided if it belongs to the most sensitive species. Therefore in a worst case approach the lowest acute LC50 is used in combination with an assessment factor of 1000 to determine the PNEC. The most sensitive acute aquatic toxicity data was obtained on *Ceriodaphnia cf. dubia*, with an EC50 (48h) equal to 277 mg/l. So, for the aquatic compartment, the calculated PNEC_{water} of sodium tripolyphosphate is 0.277 mg/l (see Table 5).

Table 5. PNEC Water

	EC50	Assessment factor	PNEC
Aquatic Organism:			
<i>Ceriodaphnia cf. dubia</i>	277 mg/l	1000	0.277 mg/l

PNEC Sediment

The PNEC_{sediment} is calculated by EUSES from the PNEC_{water} by the equilibrium partitioning method. A PNEC_{sediment} of 0.172 mg.kgwwt⁻¹ is obtained.

PNEC soil

The PNEC_{soil} is calculated by EUSES from the PNEC_{water} by the equilibrium partitioning method. A PNEC_{soil} of 0.0335 mg.kgwwt⁻¹ is obtained.

PNEC STP

The PNEC_{STP} is derived from the EC10 on activated sludge respiration by application of an assessment factor of 10.

Table 6. PNEC STP

	EC10	Assessment factor	PNEC
Inhibition of the activated sludge respiration	> 500 mg/l	10	50 mg/l

A PNEC_{STP} of 50 mg/l will be used in the risk assessment.

4.3 Environmental Risk Characterisation

The PEC and PNEC values with corresponding PEC/PNEC ratios (calculated with EUSES) are summarised in tables 7a and 7b.

Table 7a. Regional PEC/PNEC values

PEC	PNEC	PEC/PNEC = RCR
Regional PEC _{surface water} = 0.0772 mg.l ⁻¹	0.277 mg.l ⁻¹	0.279
Regional PEC _{sediment} = 0.0466 mg.kgwwt ⁻¹	0.172 mg.kgwwt ⁻¹	0.272
Regional PEC _{soil} = 1.88 10 ⁻⁵ mg.kgwwt ⁻¹	0.0335 mg.kgwwt ⁻¹	5.6 10 ⁻⁴

Table 7b. Local PEC/PNEC values

PEC	PNEC	PEC/PNEC = RCR
Local PEC _{surface water} = 0.694 mg.l ⁻¹	0.277 mg.l ⁻¹	2.5
Local PEC _{sediment} = 0.546 mg.kgwwt ⁻¹	0.172 mg.kgwwt ⁻¹	3.18
PEC _{micro-organisms/STP} = 6.16 mg.l ⁻¹	50 mg.l ⁻¹	0.123
Local PEC _{soil} = 2.4 10 ⁻³ mg.kgwwt ⁻¹	0.0335 mg.kgwwt ⁻¹	0.0715

4.3.1 Aquatic compartment

The calculated PEC/PNEC ratios in the regional surface water and in the local surface water, using EUSES computer program, are respectively 0.279 and 2.5. The local RCR > 1 in water is due to the application of the 1,000 assessment factor to the available acute toxicity data, in the absence of a sound chronic toxicity data.

4.3.2 Sediment

The calculated PEC/PNEC ratios in regional sediment and in local sediment, using EUSES computer program, are respectively 0.272 and 3.18. The local RCR > 1 in sediment is due to the application of the 1,000 assessment factor to the available acute toxicity data, in the absence of a sound chronic toxicity data.

4.3.3 Sewage treatment plant

The calculated PEC/PNEC ratio for STP is found to be 0.123. This ratio is below 1 and so does not indicate a risk.

4.3.4 Soil compartment

Regional and local PEC/PNEC ratios for the soil compartment are below 1, and thus do not indicate a risk.

4.3.5 Conclusion

No environmental risk related to STPP use in detergents is indicated in soil, air or sewage treatment plants.

The PEC/PNEC ratios are >1 in the local exposure scenarios for the water and sediment compartments (2.5 and 3.18 respectively). These scenarios do not take account of the effects of implementation of EU sewage treatment legislation (Directives 91/271 and 2000/60) requiring tertiary sewage treatment and, hence, a considerable reduction of STPP and phosphate in plant effluents. Therefore, the present risk assessment may be overly conservative for many areas in Europe.

STPP has been used for many years. It is an authorised food and drug additive. It did not show any acute toxicity effect to the aquatic organisms tested, as all EC/LC50 are above 100 mg/l, and, consequently, no chronic toxicity studies have been conducted on aquatic species. This lack of a sound chronic data implies the application of an assessment factor of 1000 to the acute toxicity data. It is very probable that the PEC/PNEC ratios >1 obtained for the local water and sediment scenarios are simply the consequence of the conservatism of the PNEC derivation from acute toxicity studies.

To refine the aquatic PNEC of STPP, CEEP (Centre Européen d'Etudes des Polyphosphates) has planned acute toxicity tests on *Daphnia magna* and *Ceriodaphnia dubia*, as well as a chronic toxicity test on the most sensitive species if necessary.

4.4 Preliminary risk characterisation of orthophosphate formed from STPP hydrolysis

The environmental aspects of orthophosphate which is the final hydrolysis product of STPP have not been addressed explicitly in this HERA risk assessment. Nevertheless, a preliminary risk characterisation based on simplified but conservative assumptions was conducted to assess the possible environmental impact of STPP-based orthophosphate in terms of ecotoxicological effects.

Given that all the STPP emitted through detergent consumption is hydrolysed into orthophosphate and considering that orthophosphate is eliminated on average to 40% in mechanical-biological WWTPs (see § 4.1.1.2), EUSES predicts a $PEC_{\text{regional water}}$ of 0.63 mg/l and a $PEC_{\text{local water}}$ of 2.1 mg/l of orthophosphate. These regional and local PEC_{water} are conservative but are in accordance with the concentration 0.2-1.2 mg/l of total phosphorus generally measured in the European rivers (see § 4.1.3), *i.e.* 0.6-3.7 mg/l expressed as orthophosphate, which includes the natural background concentration and all the anthropogenic sources from municipal and agricultural contributions.

This conservative $PEC_{\text{local water}}$ can be compared with the level of orthophosphate present in reconstituted test water used in several long-term ecotoxicity studies by Rosen et al. (2001). The basic concentration of orthophosphate in this ecotoxicity test media is equal to 3 mg/l and should represent a figure which is a conservative equivalent of a PNEC, *i.e.* a phosphate concentration which will not have any toxic effect to aquatic organisms. As this PNEC is higher than the calculated $PEC_{\text{local water}}$, *i.e.* $PEC/PNEC < 1$, it is justified to conclude that

orthophosphate resulting from the hydrolysis of STPP does not present a risk for the aquatic environment.

4.5 Eutrophication

This targeted environmental risk assessment of STPP addresses the issues of toxic effects to biota in the environmental compartments. An additional environmental issue concerning phosphates in general, and therefore also STPP, is their role in the nutrient enrichment of surface waters (eutrophication).

As shown in this report, STPP is hydrolysed ultimately to soluble inorganic phosphates (orthophosphate PO_4^{3-}) or transformed to insoluble inorganic forms. These are the same phosphates as those formed by natural hydrolysis of human urine and faeces, animal wastes, food and organic wastes, mineral fertilisers, bacterial recycling of organic materials in ecosystems, etc.

Factors involved in eutrophication

Phosphates are an essential nutrient (food element) for plants, and stimulate the growth of water plants (macrophytes) and/or algae (phytoplankton) if they represent the growth-limiting factor. In some cases, nutrient enrichment (fertilisation) of surface waters will be absorbed by the food chain (grazing by zooplankton, which are in turn consumed by fish), leading to increased fish catches. The ecosystem effect is thus dependent on factors such as zooplankton grazer population and distribution, or toxicants which might affect these populations. In other cases, nutrient enrichment of a given ecosystem will have no apparent effect, because algal development is limited by other factors. However, in certain circumstances, nutrient enrichment can lead to negative effects, ranging from ecosystem modifications, through algal blooms, to in extreme cases (through decomposition of plant biomass) oxygen depletion and collapse of the biocenosis in a surface water.

A large proportion of Europe's surface waters are currently subject to anthropogenic nutrient enrichment, with the largest fluxes of both phosphates and nitrates coming from agriculture (animal wastes, fertilisers, soil erosion) and human sewage. This is a serious environmental issue. Requirements to reduce phosphate and nutrient fluxes from sewage (of which, detergents where used are a minority proportion of phosphates) are directly addressed by the EU Urban Wastewater Treatment Directive 91/271/EEC.

The contribution of detergent phosphates (STPP) to the environmental effects of nutrient enrichment cannot be addressed by a risk assessment type approach for the reasons outlined below, and is therefore not addressed by this report.

Where reducing sewage inputs of phosphates into surface waters is expected to contribute to reducing problems related to nutrient enrichment (in the context of agricultural and other nutrient loadings), then sewage collection and treatment including phosphorus removal will be necessary, irrespective of whether or not STPP is used in detergents. No cases have been documented where reducing detergent phosphates only has resulted in identifiable environmental improvements.

Why a risk assessment methodology is not applicable to nutrient enrichment

The risk assessment methodology is based on a comparison between PEC (predicted environmental concentration) and PNEC (predicted no effect concentration).

However, the key obstacle is that a PNEC related to nutrient disturbance cannot be defined for a chemical, and in particular for phosphates. The ecosystem reaction to increased phosphate concentrations depends on many factors which vary spatially and temporally. A water body will react to additional phosphate input if it is the growth-determining factor, while temperature, light, low water-flow, concentrations of other nutrients (nitrogen, iron, oligo-elements) and ecosystem balance (grazer populations) may also have an impact on plant or algal development depending on the specific situation.

“No effect” or “effect” of an increase in phosphate loadings to a given part of a water body may thus be dependent on a number of other factors: is plant/algal development being limited in the present circumstances by phosphate availability in the water? or is it being limited by other nutrients or by other factors?

A “No effect concentration” thus cannot be defined, neither in theory, nor by any form of practical or field “assay” or test. The results will in each case depend directly on the other parameters set for the test: concentrations of other nutrients, light, temperature, algal and grazer species and density. It is therefore not possible to derive a PNEC in terms of eutrophication.

5 Human health assessment

5.1 Consumer Exposure

5.1.1 Product Types

Data supplied by the formulating companies indicate that sodium tripolyphosphate (STPP) is used in regular and compact fabric washing products, laundry additives, automatic dishwashing products, and in hard surface and toilet cleaners.

The table below indicates typical STPP concentrations in household detergents (AISE, 2000) :

Table 8 : STPP concentrations (%) in household detergents for year 2000.

	Min.	Max.	Typical
LAUNDRY REGULAR			
Powder	10	43	20-25
Liquid	1	21	1-21
LAUNDRY COMPACT			
Powder	25	40	30-33
Liquid/gel	10	32	18-30
Tablet	30	63	40-47
FABRIC CONDITIONERS			
Others (refresher spray)	0.1	0.1	0.1
LAUNDRY ADDITIVES			
Liquid Bleach	0.05	0.1	0
MACHINE DISHWASHING			
Powder	15	55	25-40
Liquid	20	30	24-30
Tablet	15	60	20-51
Gel	15	30	15-30
SURFACE CLEANERS			
Liquid	1	2	1
Powder	7	30	7-30
TOILET CLEANERS			
Powder	1	1	1

5.1.2 Consumer Contact Scenarios

Based on the product types, the consumer contact scenarios to STPP in household cleaning products were identified as follows:

- Dermal contact:
 - Direct skin contact during laundry hand-wash and surface cleaning with solutions prepared from powder, liquid, gel or tablets
 - Direct skin contact during laundry pre-treatment (paste powder, liquid/gel)

- Direct skin contact with solid (powder, tablets)
- Indirect skin contact via residues on textiles
- Oral ingestion:
 - Indirect exposure via the environment (drinking water and eating food)
 - Exposure via ingestion of residues deposited on dishes
- Contact via inhalation:
 - Handling the powder formulations of detergent dust or using spray refreshers
- Other sources of exposure
 - Accidental or intentional overexposure

5.1.3 Consumer Exposure Estimate

There is a consolidated overview concerning habits and uses of detergents and surface cleaners in Western Europe that was issued by A.I.S.E. (2002). This table reflects the consumer's use of detergents in g/cup, tasks/week, duration of task and other uses of products. The relevant data from that table were used to calculate the following exposure estimates.

5.1.3.1 Contact from hand washing laundry with solutions containing STPP

Skin contact can occur during hand washing of clothes with laundry detergent.

- the highest concentration of laundry detergents in hand-wash solutions is assumed to be approximately 1% (i.e. 10 mg/ml) (AISE, 2002).
- The highest concentration of STPP in laundry additives (liquid bleach) is 0.1% (1 mg/ml). The highest concentration of liquid bleach in hand wash solution is 1%, so the amount absorbed percutaneously from hand wash would be approximately 0.01 mg/ml, and is therefore considered negligible.
- Among the various categories (powder, liquid, gel or tablets, either regular or compact), the highest concentration of STPP in laundry detergents is 63% (630 mg/ml) present in laundry compact tablets (AISE, 2000). In this case, the highest concentration of STPP in hand washing solution using laundry tablets would result in an estimated exposure of 6.3 mg/ml per task. However, powder detergents are more frequently used for laundry (maximum use: up to 21 tasks a week) than liquid and tablets (maximum use: up to 10 tasks a week) (AISE, 2002). Thus, because the use of powder would result in a higher daily exposure, it was taken as worst case in the following calculations. The highest concentration of STPP in powder laundry detergents is 40% (400 mg/ml), which would result in an estimated exposure of 4 mg/ml per task.
- contact of hands and forearms into solution would expose a maximum of 1980 cm² of skin surface (Vermeire et al., 1993; TGD, 1996).
- The amount of STPP absorbed via the skin can be calculated from the STPP concentration applied, surface area of hands and forearms exposed, film thickness, and

fraction absorbed, using the exposure model of the HERA guidance document (2002). The following assumptions were made:

- a film thickness of 100 μm (0.1 mm or 0.01 cm) of solution is assumed to remain on the hands (Vermeire et al., 1993; TGD, 1996)
- because ionic substances are considered to be less easily absorbed than non-ionic compounds (Schaeffer and Redelmeier, 1996), a percutaneous absorption of 1% in 24 hour exposure time was used as a worst case assumption in this assessment
- the worst case assumption is that 100 % of the product remain on the skin (no wiping or rinsing).

C_{STPP} = maximum product concentration, in mg/cm^3 :	4.0 mg/ml = 4.0 mg/cm ³
T_{der} = the thickness of product layer in contact with skin, in cm :	100 μm = 0.01 cm
S_{der} = surface area of exposed hands, in cm^2 :	1980 cm ²
F = % weight fraction absorbed via skin in a 24 hour period :	1% = 0.01

Systemic exposure, in mg :

$$\begin{aligned} \text{EXPsys} &= C_{STPP} \times T_{der} \times S_{der} \times F \\ \text{EXPsys} &= 4.0 \text{ mg}/\text{cm}^3 \times 0.01 \text{ cm} \times 1980 \text{ cm}^2 \times 0.01 \\ \text{EXPsys} &= \text{approx. } 0.792 \text{ mg STPP absorbed in 24 hours} \end{aligned}$$

With the very conservative assumptions of a 10-min contact time per task and a maximum task frequency of 21 hand washes per week (= 3 tasks a day) (AISE, 2002), the total daily contact time is 30 minutes.

Therefore, the daily contact can be calculated as $[(0.8 \text{ mg}/\text{day}) \times (30/60) \times (1/24)]$ yielding an assumed absorption of 0.0165 mg per day.

Based on a body weight of 60 kg, the systemic dose of STPP would be equal to $0.0167 / 60 = 0.275 \times 10^{-3} \text{ mg}/\text{kg}$ body weight/day, i.e. **0.3 $\mu\text{g}/\text{kg}/\text{day}$** .

5.1.3.2 Contact from pre-treatment of clothes with products containing STPP

Skin contact can occur during spot-treatment with a detergent paste (60% paste, or 600 mg/ml powder), liquid, gel, or liquid bleach used neat (AISE, 2002).

- The highest concentration of STPP in liquid bleach is 0.1% (1 mg/ml). In case liquid bleach is used neat as laundry pre-treatment, the resulting estimated hand exposure is 1 mg/ml.

The highest concentration of STPP in powder laundry detergents (compact) is estimated to be 43% (430 mg/ml) (AISE, 2000). Therefore, the highest concentration of STPP in the hand washing paste prepared from powder at approximately 60% (AISE, 2002) is approximately 258 mg/ml.

The highest concentration of STPP in liquid/gel detergents is 32% (320 mg/ml). In case liquid or gel is used neat as laundry pre-treatment, the resulting estimated hand exposure is 320 mg/ml. However, because powder is used more frequently than liquid or tablets (21 tasks per week for powder, and 10 tasks a week for liquid or tablets) (AISE, 2002) and therefore would result in a higher daily exposure, the use of powder detergents is taken as worst case in the following calculations.

- Direct contact of hands would expose a maximum of 840 cm² (Vermeire et al., 1993; TGD, 1996) of the skin surface.
- The amount of STPP absorbed via the skin can be calculated from the STPP concentration applied, surface area of hands exposed, film thickness, and fraction absorbed, using the exposure model of the HERA guidance document (HERA, 2002). The following assumptions were made:
 - a film thickness of 100 µm (0.1 mm or 0.01 cm) on the hands (Vermeire et al., 1993; TGD, 1996);
 - a percutaneous absorption of 1% for ionic substances in 24 hour exposure time was considered as a worst case, on the assumption that ionic substances are less easily absorbed than non-ionic compounds (Schaeffer and Redelmeier, 1996);
 - the worst case assumption is that 100 % of the product remain on the skin (no wiping or rinsing).

C_{STPP} = maximum product concentration, in <i>mg/cm³</i> :	258 mg/ml = 258 mg/cm ³
T_{der} = the thickness of product layer in contact with skin, in <i>cm</i> :	100 µm = 0.01 cm
S_{der} = surface area of exposed hands, in <i>cm²</i> :	840 cm ²
F = % weight fraction absorbed via skin in a 24 hour period :	1% = 0.01

Systemic exposure, in *mg*:

$$\begin{aligned} \text{EXPs}_{\text{sys}} &= C_{STPP} \times T_{der} \times S_{der} \times F \\ \text{EXPs}_{\text{sys}} &= 258 \text{ mg/cm}^3 \times 0.01 \text{ cm} \times 840 \text{ cm}^2 \times 0.01 \\ \text{EXPs}_{\text{sys}} &= 21.67 \text{ mg STPP absorbed in 24 hours} \end{aligned}$$

With the very conservative assumptions of a 10-min contact time per task and a task frequency of 21 tasks pre-treatment wash per week using powder (AISE, 2002), the total daily contact time is 30 minutes.

Therefore, the daily exposure can be calculated as [(21.7 mg/day) x (30/60) x (1/24)] yielding an assumed absorption of 0.45 mg per day.

Based on a body weight of 60 kg, the estimated systemic dose of STPP resulting from laundry pre-treatment would be equal to $0.45 / 60 = 7.5 \times 10^{-3}$ mg/kg body weight/day, or **7.5 µg/kg bw/day**.

5.1.3.3 Contact from laundry or automatic dishwashing products (powder, tablets)

STPP is present in detergents used for laundry detergents (machine or hand-washing products) and in products for automatic dishwashers, but it is not present in hand dishwashing formulations (AISE, 2000).

Direct contact with powder or tablets may occur when handling the solid product to place it into the laundry washer, preparing hand wash solution for clothes, or when loading dishwashing detergent in the automatic dishwasher. Contact time is usually very short (less than 1 minute) (AISE, 2002), and the skin area in contact is limited. The resulting uptake of STPP is assumed to be negligible under these conditions, and it is not expected to impact the overall exposure.

5.1.3.4 Contact from surface cleaning with detergent products containing STPP

Skin contact can occur during surface cleaning with a detergent solution containing sodium tripolyphosphate.

- the highest concentration of liquid surface cleaners used in a volume of wash water of 5 liters is 110 g per task, resulting in a maximum concentration of 22 g/l of detergent in water (AISE, 2002). The highest concentration of STPP in liquid surface cleaners is estimated to be 2% (AISE, 2000). Therefore, the amount of STPP in the wash water used for surface cleaning is 0.44 g/l (0.44 mg/ml).
- the highest concentration of powder surface cleaners used in a volume of wash water of 5 liters is 40 g per task, resulting in a maximum concentration of 8 g/l of detergent (AISE, 2002). The highest concentration of STPP in powder surface cleaners is estimated to be 30% (300 mg/ml) (AISE, 2000). Therefore, the amount of STPP in the wash water used for surface cleaning is estimated to be 2.4 g/l (2.4 mg/ml). This figure is taken as worst case value in the calculation.
- direct contact of hands and forearms into the wash water solution would expose a maximum of 1980 cm² (Vermeire et al., 1993; TGD, 1996) of the skin surface.
- The amount of STPP absorbed via the skin can be calculated from the STPP concentration applied, surface area of hands exposed, film thickness, and fraction absorbed, using the exposure model of the HERA guidance document (HERA, 2002), and using the following assumptions:
 - a skin thickness of 100 µm (0.1 mm or 0.01 cm) of solution on the hands (Vermeire et al., 1993; TGD, 1996);
 - because ionic substances are considered to be less easily absorbed than non-ionic compounds (Schaeffer and Redelmeier, 1996), a percutaneous absorption of 1% in 24 hour exposure time was used as a worst case assumption in this assessment;
 - the worst case assumption is that 100 % of the product remain on the skin (no wiping or rinsing).

$$EXP_{sys} = C_{STPP} \times T_{der} \times S_{der} \times F_1 \times F_2$$

C_{STPP} = maximum substance concentration, in mg/cm ³ :	2.4 mg/ml = 2.4 mg/cm ³
T_{der} = the thickness of product layer in contact with skin, in cm:	100 µm = 0.01 cm.
S_{der} = surface area of exposed hands and forearms, in cm ² :	1980 cm ²
F_1 = percentage (%) weight fraction remaining on skin	100% (worst case)
F_2 = % weight fraction absorbed via skin in a 24 hour period :	1% = 0.01

$$EXP_{sys} = C_{STPP} \times T_{der} \times S_{der} \times F$$

$$EXP_{sys} = 2.4 \text{ mg/cm}^3 \times 0.01 \text{ cm} \times 1980 \text{ cm}^2 \times 0.01$$

$$EXP_{sys} = 0.47 \text{ mg STPP absorbed in 24 hours}$$

Under the very conservative assumptions of 20 min contact time per task and a task frequency of 7 tasks per week (AISE, 2002) (1 task a day), the total daily contact time is 20 minutes. Therefore, the daily contact can be calculated as [(0.47 mg/day) x (20/60) x (1/24)], yielding an assumed absorption of 0.0165 mg per day.

Based on an average adult body weight of 60 kg the systemic dose of STPP during the task of surface cleaning would be equal to $6.52 / 60 = 0.1 \mu\text{g/kg bw/day}$.

5.1.3.5 Contact from toilet cleaning with product containing STPP

Skin contact can occur during the cleaning of the lavatory pan with a detergent containing sodium tripolyphosphate. This is commonly a powder, containing a maximum of 1% STPP (AISE, 2002).

Investigations on uses and consumer in-home observations have shown that most people pour the toilet cleaner directly into the lavatory pan (Weegels and van Veen, 2001). Contact time is estimated to be very short (less than 1 minute) (AISE, 2002), and the skin area in contact is expected to be limited. The resulting uptake of STPP is assumed to be negligible.

5.1.3.6 Indirect skin contact via wearing clothes

Residues of components of laundry detergent may come into contact with the skin as a consequence of wearing clothes.

STPP is very soluble (see chapter 3 on Substance Characterisation), therefore only a minimal amount of the substance is expected to be deposited in solid form on clothes after washing and rinsing, and to come in contact with the skin via wearing textile.

Assuming a worst case scenario, the exposure to STPP can be estimated according to the following calculation (HERA, 2002):

$$\text{EXPs}_{\text{sys}} = FI \times C'_{\text{STPP}} \times S_{\text{der}} \times n \times F_2 \times F_3 \times F_4 / BW$$

FI = % weight fraction of substance in product: 1 (not used)

C'_{STPP} = amount of STPP in contact with skin surface via fabric wash and wear, in mg/cm^2 :

C' is determined multiplying the amount of STPP deposited on 1kg of fabric after 25 repeats of washing process with a typical laundry detergent times an estimated value of the fabric density ($FD = 10 \text{ mg/cm}^2$) (P&G unpublished internal data, 1996).

$$C' = F' \times FD$$

F' represents the amount of substance deposited on 1 kg of fabric. A publication has reported cumulated amounts of phosphorus residues left on textiles (polyester or cotton) after 25 machine washes using various types of phosphate-containing detergents (no further details) (Matthies et al., 1990). However, washing conditions and detection method used are not clear. Depending on fabrics, washing conditions, type of detergent, the residues measured as phosphorus varied from 9 to 800 ppm (on polyester) to 17 to 12000 ppm (i.e. 1.2%, on cotton). Phosphorus accounts for 25.3% of the STPP molecule. Assuming that all the phosphorus detected originates from STPP, the maximum amount of STPP residues left on 1 kg of fabric after 25 washes would be up to 4.74% (i.e. 0.0474 mg STPP/mg of fabric), which is a very conservative value.

FD : fabric density in mg/cm^2 10 mg/cm^2 (P&G data, 1996)

$$C' = (4.74 / 100) \times 10 \text{ mg/cm}^2 = 0.474 \text{ mg/cm}^2$$

S_{der} = surface area of exposed skin, in cm^2 : 17600 cm^2

(excluding head and hands, Vermeire et al., 1993)

n product use frequency, in *number of events per day* 1 (not used)

<i>F2</i> % weight fraction transferred from medium to skin	1% (default value, Vermeire et al. 1993)
<i>F3</i> percentage (%) weight fraction remaining on skin	100% (worst case)
<i>F4</i> percentage (%) weight fraction absorbed via skin	1% (default value taken for ionic substances, on the assumption that, according to Schaeffer and Redelmeier (1996), ionic substances are less easily absorbed than non-ionic compounds);
<i>BW</i> body weight, in <i>kg</i>	60 kg

$$EXP_{sys} = [0.474 \text{ mg/cm}^2 \times 17600 \text{ cm}^2 \times 1 \times 0.01 \times 1 \times 0.01] / 60 \text{ kg}$$

$$EXP_{sys} = 0.0139 \text{ mg/kg/d} = \mathbf{14 \mu\text{g/kg/day}}$$

5.1.3.7 Oral exposure via the environment (drinking water and food)

- Indirect oral exposure to STPP can occur through drinking water processed from surface water, and through eating food where STPP may have accumulated. This estimate was made excluding the potential intake of STPP which is otherwise used as direct food additive. The concentration in drinking water is estimated to be equal to the regional PEC in surface water as obtained in section 4 (Environmental risk assessment), i.e. 0.0772 mg/l. As a worst case scenario, it is assumed that there is no water treatment to eliminate STPP from the drinking water. It is further assumed a complete intestinal absorption, and based on a daily water consumption of 2 liters for an adult of 60 kg (TGD, 1996), the daily intake of STPP is estimated to be:

$$EXP_{sys \text{ drinking water}} = (\text{PEC}_{\text{regional}} \times \text{Volume water ingested/day}) / \text{body weight}$$

$$EXP_{sys \text{ drinking water}} = (0.077 \text{ mg/l} \times 2 \text{ l}) / 60 \text{ kg} = 0.0026 \text{ mg/kg/day} = \mathbf{2.6 \mu\text{g/kg bw/day}}$$

- Oral intake from food was estimated with EUSES model. The Environmental Risk Assessment (section 4) indicated no significant uptake in the soil compartment. Exposure output from EUSES model also showed negligible concentrations in meat, milk and plants, resulting in a negligible daily uptake. Taking into account the potential bioconcentration in fish and assuming a default value for daily consumption of 0.115 kg fish/day (TGD, 1996), the daily dose of STPP through intake of fish (regional value) was estimated to be **0.2 $\mu\text{g/kg bw/day}$** for a 60-kg adult.

5.1.3.8 Oral exposure via residues on dinnerware

Oral exposure to STPP from household cleaning products can occur from residues on utensils and dinnerware washed using dishwashing detergents. STPP is present in detergents used for automatic dishwashers but not in hand dishwashing products (AISE, 2000). Oral exposure to STPP can result from residues on eating utensils and dishes.

The highest concentration of dishwashing detergent is 50 g per task for the machine dishwashing tablets (HERA, 2002). The highest concentration of STPP in dishwashing detergents is 60%, also in machine dishwashing tablets (AISE, 2000).

The daily exposure to STPP from eating with utensils and dishware that have been washed with products containing STPP can be estimated according to the recommended calculation assuming a worst case scenario as follows (HERA, 2002):

$$EXP_{sys} = F1 \times C' \times Ta' \times Sa \times F'' \times n \times F9 / BW$$

- $F1$ = percentage (%) weight fraction of STPP in product: 60% (dishwasher tablets)
- C' the product concentration (in mg/ml) in the dishwash solution which can remain on the surface of the article was determined dividing the amount of product per task over the wash water volume. The worst case assumption for product use is a maximum amount of 50 000 mg dishwashing detergent per task (AISE, 2002). According to manufacturers, the average wash water volume used by current automatic dishwashers in Europe is about 18 liters (18 000 ml). The resulting estimated value is 2.77 mg/ml.
- Ta' amount of water left on dishes after washing and rinsing. The dish surface (including dishes, utensils, glassware, pans etc...) in contact with food and used by one individual each day is the equivalent of 5400 cm². The amount of wash water left on non-rinsed dishware was estimated to amount 3 ml for this surface of 5400 cm², i.e. 0.00055 ml/cm². With a factor 10 for rinsing, the amount of water left on dinnerware is 0.000055 ml/cm² (JORF, 1990; ECETOC, 1994).
- Sa surface area of article exposed to substance, in cm²: 5400 cm² (JORF, 1990)
- F'' percentage (%) weight fraction transferred from article and ingested 100% (worst case)
- n product use frequency, in *number of events per day* 1 (AISE, 2002)
- $F9$ percentage (%) weight fraction absorbed or bioavailability 100% = 1 (default value)
- BW 60 kg for an adult.

$$EXP_{sys} = [(60/100) \times (2.77 \text{ mg/ml}) \times (0.000055 \text{ ml/cm}^2) \times (5400 \text{ cm}^2) \times 1 \times 1 \times 1] / 60$$

$$EXP_{sys} = 0.0082 \text{ mg/kg/day} = \mathbf{8.2 \mu\text{g/kg/day}}$$

5.1.3.9 Inhalation exposure

Inhalation exposure to STPP in detergents is expected to be negligible because consumer products consist of agglomerates or crystals, and dust formation is very small. STPP is not lost from liquid products to the air. This was also noted in an experimental acute inhalation study in rats, where the maximum attainable concentration of dust that could be generated was limited to 0.39 mg/l (FMC, 1990).

The pouring of powdered laundry detergent has been estimated to release 0.27 µg dust per cup of detergent used for machine laundering (van de Plassche et al. 1999), of which up to 43%, or 0.12 µg/use is STPP (AISE, 2000). This amount is not considered to contribute significantly to the total exposure to STPP.

In the worst case assumptions that all the dust is inhaled during machine loading and that this task is performed up to 3 times a day, the exposure to STPP of an adult with an average body weight of 60 kg is estimated to be:

$$EXP_{sys} \text{ (dust inhalation)} = [0.12 \mu\text{g/use} \times 3] / 60 \text{ kg} = 0.06 \mu\text{g/kg/day}$$

The assumption of a similar figure (0.27 µg dust per cup) with machine dishwashing powder, which contain up to 55% STPP (AISE, 2000), would result in a maximum uptake of 0.15 µg/use STPP. In the worst case assumptions that all the dust is inhaled during machine loading and that this task is performed up to once a day, the exposure to STPP of an adult with an average body weight of 60 kg is estimated to be:

$$EXP_{sys} \text{ (dust inhalation)} = [0.15 \mu\text{g/use} \times 1] / 60 \text{ kg} = 0.0025 \mu\text{g/kg/day}$$

STPP can also be present in refresher sprays used for ironing of fabrics, at a maximum concentration of 0.1% (AISE, 2000). STPP is not frequently used in this type of products in Europe. Information from formulators indicated that the size of airborne particles generated from spray products is expected to be well above 10 µm, and therefore not considered to be in the respirable fraction. Because the use of STPP in such products is rather limited and is considered to result in limited exposure to inhalable particles, it can be estimated that the exposure to STPP from refresher sprays is negligible as compared to other product types.

Therefore, total exposure from inhalation route is estimated to be below **0.1 µg/kg/day**.

5.1.3.10 Total Consumer exposure (all routes) from household cleaning products

1- Dermal

Hand washing laundry:	0.3 µg/kg/day
Fabric pre-treatment:	7.5 µg/kg/day
Pouring product:	negligible
Surface cleaning:	0.1 µg/kg/day
Wearing laundered fabric:	14 µg/kg/day
Total dermal:	21.9 µg/kg/day

2- Oral

Uptake via drinking water:	2.6 µg/kg/day
Uptake via food (fish):	0.2 µg/kg/day
Residues on dishes:	8.2 µg/kg/day
Total oral exposure:	11 µg/kg/day

3- Inhalation

Pouring laundry detergent:	< 0.1 µg/kg/day
Pouring dishwashing detergent:	negligible
Use of refresher spray:	negligible
Total inhalation:	< 0.1 µg/kg/day

Total exposure via all routes: 33 µg/kg/day

5.1.3.11 Accidental or intentional overexposure

Accidental or intentional overexposure to STPP may potentially occur via household detergents, and by various routes. Two main routes of accidental exposure should be considered.

Eye exposure

Accidental eye exposure to STPP may occur through splashing of a detergent solution, while handwashing clothes, dishwashing, or brushing the lavatory pan, or from handling powder. Therefore, the eye irritation potential should be considered in the context of accidental exposure.

Oral exposure

Oral exposure can occur following ingestion of detergent products containing sodium tripolyphosphate, or solutions of these products in water. Detergent products usually contain bitter agents to discourage children from drinking them. Therefore, most accidental ingestions of laundry or dishwashing products by young children involve small amounts of products (1 teaspoon or less) (Petersen, 1989). However, in some cases, determined adult can overcome the bitter taste and consume toxic quantities.

To the best of our knowledge, no cases of poisoning or toxicity have been reported in the literature for sodium tripolyphosphate. Based on a case that occurred with sodium phosphate at high dose, symptoms are expected to be similar to those from a phosphate poisoning: hypocalcaemia and metabolic disturbance, and respiratory distress (Vincent and Sheikh, 1998).

5.2 Hazard Assessment

5.2.1 Summary of available toxicological data

5.2.1.1 Acute Toxicity

Acute oral toxicity

Four acute toxicity studies in rats were considered reliable: one study was considered valid without restriction, and three were valid with restriction (FMC, 1997; Hoechst, 1966; Smyth et al. 1969; Stauffer, 1971). Only one study complied with GLP regulations. Some of the restrictions includes the following: in some of these studies, animals of only one sex were used, and clinical observations were not always documented. However, the study design of all the studies included at least 5 animals per dose group.

The most reliable study was a limit study at 2000 mg/kg STPP in 5 rats of each sex, well-documented and conducted according to GLP and the OECD guideline 401 (FMC, 1997). No mortality occurred. At 2000 mg/kg, clinical signs were limited to abdomino-genital staining, decreased locomotion, and diarrhoea. All signs resolved within 24 hours post-dosing. All rats gained weight by day 14 of the study. At necropsy, no gross internal lesions were noted in any of the animals.

In a second study (Stauffer, 1971), 5 male Sprague-Dawley rats per dose group were administered the test material (sodium tripolyphosphate, anhydrous) as a 20% solution in water, at 464, 1000, 2150 and 4640 mg/kg, by gavage. This study was not performed according to GLP. The animals were observed for 14 days after treatment for mortalities and signs of toxicity.

No mortality occurred at the 3 lowest doses, and 2 animals died in the group treated at 4640 mg/kg. Clinical signs included acute depression, nasal discharge, dyspnea, and gasping. Gross pathology of the dead animals showed gross gastrointestinal haemorrhage, with congestion of the kidneys, adrenals, liver, lungs and heart. Based on these results, the LD50 was calculated to be 5010 mg/kg for male rats.

The acute oral LD50 for rats in the other studies were 3100 mg/kg bw for female rats (Hoechst, 1966), and 6500 mg/kg bw for male rats (Smyth et al. 1969). Additional sources

reported in secondary literature, and for which the reliability was not assignable, indicated results that were usually consistent with these figures in rats, mice, rabbits and dogs with LD50 values ranging from > 800 mg/kg (highest dose tested in that dog study) to 5190 mg/kg bw (IUCLID, 2000a; Weiner et al., 2001).

Based on these results, STPP is considered of low acute toxicity potential by the oral route.

Acute inhalation toxicity

Only one report was available on inhalation toxicity with whole-body exposure (FMC, 1990). This study was performed according to GLP and US EPA FIFRA Regulation OPP 81-3 test guidelines. A group of 5 male and 5 female Wistar rats was exposed continuously for 4 hours to a test atmosphere containing dust generated from STPP (purity > 90%) at the maximum attainable concentration of 0.39 mg/l. A second group received clean air only for the same period and served as a control. Observations for signs of toxicity were conducted during exposure and twice daily following exposure throughout the 14-day observation period. Body weight, food and water consumption were recorded daily.

No death occurred. During exposure, clinical signs were consistent with exposure to an irritant dust: partial closing of the eyes, exaggerated respiratory movements, restless behaviour and excessive grooming. No other clinical signs were observed during the observation period. Residues of test substance were noted on fur of the exposed rats. Weight loss was observed in treated rats, especially male rats where it was statistically significant. Food consumption was reduced for 1 day in male rats and slightly reduced for 1 day in females. Water consumption was slightly reduced for 1 day in male rats. At necropsy, the lung weight to body weight ratio for all rats was within normal range. Grey areas were seen on the lung of 1 treated male rat. No macroscopic abnormalities were observed in any other rat.

The nominal concentration calculated from the gross weight of STPP dispersed and the total volume of air supplied to the system was in excess of 24 mg/l of air. The mean concentration in air, determined gravimetrically, was 0.39 mg/l (standard deviation: 0.120 mg/l) and was the maximum attainable air concentration. The mean mass median aerodynamic diameter was not determined in the study, but the majority of the particles had a size above 5.5 µm (largest filter size). Approximately 27% by weight of particles were less than 5.5 µm in aerodynamic diameter (mean % respirable from 2 samples).

The inhalation study available indicated that dust formation is relatively small. At the maximum attainable air concentration of 0.39 mg/l, no significant toxicity was observed in rats.

In addition, review of studies performed on a range of inorganic phosphates tends to support a low potential toxicity via the inhalation route for these compounds (LC50 ranged from > 0.39 to > 5.06 mg/l) (Weiner et al., 2001).

Acute dermal toxicity

One study was available for review (Stauffer, 1971). This study was performed before the application of GLP. STPP (anhydrous, purity not specified) was applied neat at 4640 mg/kg to a clipped area of intact abdominal skin of 4 New Zealand white rabbits, under an occlusive dressing, for 24 hours. After removal of the dressing, examinations were performed for 14 days. A control group was not included. No death occurred. No apparent signs of toxicity were observed in any of the test animals. Moderate erythema was observed at the site of treatment. The acute dermal LD50 was therefore higher than 4640 mg/kg. Despite some restrictions with regard to methodology documentation, the test results were considered reliable.

Additional data reported in secondary literature (original reports not assessed) also supported low acute dermal toxicity in rabbits (LD50 ranging from 2900 to >7940 mg/kg) (Weiner et al., 2001).

Conclusion for acute toxicity

Acute oral and dermal toxicity studies performed in compliance with standard methods and considered reliable with and without restrictions indicated LD50 values above 2000 mg/kg by either route. Additional studies reported in secondary literature also supported low acute oral and dermal toxicity.

One reliable study was available on acute inhalation toxicity, in which no death was observed at the maximum attainable air concentration of 0.39 mg/l. In addition, review of studies performed on a wide range of inorganic phosphates indicates a low potential for acute inhalation toxicity for these compounds.

The experimental data show a low acute toxicity potential for sodium tripolyphosphate.

5.2.1.2 Skin irritation

The skin irritation potential of STPP was assessed in several studies which were considered reliable with restrictions, and only one was performed according to GLP and considered valid without restriction (FMC, 1989; Cannon, 1975a; Stauffer, 1971).

In the study performed according to GLP and EPA Regulation OPP 81-5 (FMC, 1989), 0.5 g technical grade STPP was moistened with saline, then applied for 4-hour under a semi-occlusive pad to 3 male and 3 female New Zealand white rabbits. Scoring was performed 30 min after removal of the patch, then daily for 3 days. These test conditions are similar to OECD Guideline 404. No erythema and no oedema were observed throughout the observation period, and the study was terminated after the 72-hour scoring. All animals gained weight and remained healthy during the study. Based on these results, STPP is not considered a skin irritant according to EC criteria laid down in Annex VI to Directive 67/548/EEC.

The tests performed according to Draize procedure used conditions more severe than the current OECD guidelines: 500 mg of neat substance applied for 24 hours under an occluded patch, on intact and abraded skin sites (Cannon, 1975a; Stauffer, 1971). Observations were performed at 24 and 72 hours. Usually 6 animals were used. In one of the studies severe reactions were observed on the abraded skin sites. In both studies only limited cutaneous effects were observed on the intact skin sites: only very slight erythema was observed at 24 hours in 2 animals out of 6, and a very slight oedema was observed in one animal at 24 hours in one of the studies. In both studies, all reactions had cleared by 72 hours.

Additional data reported in a publication not very well documented (Nixon et al, 1975) indicated that STPP applied as a 50 % (w/v) aqueous solution on the intact and abraded skin of 6 albino rabbits (sex not indicated) for 4 hours (patch application not detailed) produced no irritation on the intact skin sites. In the same study, exposure to a 50% (w/v) aqueous solution of a formulation of phosphate detergent granules containing 50% STPP produced a moderate irritation in rabbits (pH of 1% aq. solution was 10.1). Effects were of a lower intensity in guinea-pigs and in human volunteers exposed in the same conditions. In a poorly documented study (Nixon et al., 1990), STPP applied neat (0.5 g) on the intact skin of 6 albino rabbits (sex and strain not specified) for 4 hours under an occlusive patch was reported to show no cutaneous reactions at the 24-, 48- and 72-hour observation times.

Conclusion

Data from animal studies, which were considered reliable although they had slight differences with current OECD guidelines, showed low or an absence of irritating effects for the substance applied neat. Additional studies less documented indicated that STPP applied at up to 50 % in aqueous solution showed low irritation potential to the rabbit and human skin. STPP is considered at most slightly irritating to skin, with effects which are well below current EC criteria for hazard classification.

5.2.1.3 Eye irritation

One well-documented study was available (Cannon, 1975b). The study was not conducted according to GLP, but the study design was in compliance with US national standard methods and similar to OECD guideline 405. Similar results were also observed in two additional studies that were less documented and not conducted in accordance to standard methods (FMC, 1986; Stauffer, 1971).

In the most reliable study (Cannon, 1975b), the eye irritation potential was assessed using the Draize procedure (US CFR section 1500.42, Title 21). Six New Zealand rabbits were included in the study and received 100 mg of solid STPP in their left eye. The right eye remained untreated and served as a control. The eyes were not rinsed. Ocular examination was performed at 24, 48 and 72 hours following treatment, then at day 4 and 7 after the instillation. The method used is comparable to OECD guideline 405, except for a shorter observation period. No iris inflammation was observed throughout the study period. Slight corneal opacity was observed in 2 animals out of 6 at 24, 48, and 72 hours, and was still present at day 7 in one animal. Slight conjunctival redness and chemosis were also observed throughout the observation period.

One of the additional studies considered was designed as a preliminary assay performed in only 2 rabbits (FMC, 1986) and did not comply with GLP. No corneal opacity and no iritis were observed during the study. Moderate conjunctival chemosis and slight conjunctival redness were observed in the unwashed eyes at 1-hour. Chemosis was no longer present at 24 hour, and slight to mild conjunctival redness was still observed. One of the unwashed eyes still had slight conjunctival redness on day 3 and recovered by day 4.

Another study was not conducted in accordance to GLP and OECD method, and amount of product applied was lower than the one recommended in current guidelines (10 mg instead of 100 mg) (Stauffer, 1971). Detailed scores were not reported, but effects were reported to be limited to moderate to severe conjunctivitis observed in 2 out of 6 rabbits during the 72-hour observation period. No signs of irritation were observed in the other animals. It was concluded that STPP is non-irritating to the eyes.

Finally, one study with limited documentation was performed with solutions at 1% or 10% STPP (prepared supposedly in 0.9% sodium chloride; pH was not documented) and showed no signs of irritation (Hoechst, 1966).

Conclusion

The study which met criteria for reliability showed ocular effects limited to conjunctival reactions and slight and transient corneal opacity for neat sodium tripolyphosphate. These results were also consistent with additional data from 2 other less reliable studies.

Overall, ocular effects of STPP seem of low intensity when tested as a powder. It is not classifiable as eye irritant according to EC criteria.

5.2.1.4 Skin sensitisation

No experimental data were available on STPP as such, with regard to skin sensitisation potential. However, a number of experimental data were available with various detergent formulations containing STPP.

A prototype mixture containing 17.5 % STPP was tested in a Büehler test conducted according to GLP (U.S. EPA - FIFRA) guidelines (Procter & Gamble, 1999a). In the test, 20 guinea pigs (10 males, 10 females) received an irritant induction concentration of 50% of the mixture containing STPP in distilled water (8.8 % STPP concentration applied) (6 h/day, occlusive) once every seven days for a total of three applications. Fourteen days after the last induction application the animals were challenged with a 35% solution of the mixture containing STPP in distilled water (6.1% STPP concentration applied) (maximum non-irritant concentration). 10 untreated animals served as controls. None of the 20 test group animals showed any response after challenge either at the 24 h or 48 h scoring. One of the 10 control group animals showed a very slight erythema (score of 1) after 24 h. The results indicate that the test substance did not induce skin sensitisation under the conditions of this test.

Results from four Repeated Insult Patch Studies conducted in human volunteers were also available with formulations containing up to 66% STPP (Procter & Gamble, 1968, 1997, 1998, 1999b). All four tests were conducted following the same procedure: groups of volunteers (73, 97, 104 and 94, respectively) were treated with patches of an aqueous dilution of the formulation containing STPP. The final concentrations of STPP actually applied in these different tests were 0.33, 0.08, 0.06 and 0.03%, respectively. The patches were applied on the upper arms, under fully occlusive conditions for 24 hours, 3 times a week, for 3 weeks during the induction period. After a 14-17-day rest period, a 24-hour challenge patch was applied on the original and alternate arm site. In all 4 studies, all the volunteers completed the test, and there was no evidence of skin sensitisation in any of the subjects involved.

In addition, among other inorganic phosphates, phosphoric acid, H₃PO₄ (CAS: 7664-38-2) and ammonium polyphosphate, (NH₄PO₃)_n (CAS: 68333-79-9), have been assessed for skin sensitisation and they were not found to cause skin sensitisation reactions in human or guinea-pigs (unpublished reports, citation in Weiner et al. 2001, IUCLID, 2000b).

Conclusion

There were no data available from standard assays to assess sensitisation potential of STPP as such. But results of a Büehler test in guinea-pigs and Repeated Insult Patch Tests in human volunteers conducted with various detergent formulations containing STPP showed no evidence of sensitisation potential.

5.2.1.5 Repeated dose toxicity

Sodium Tripolyphosphate (Curafos) was assessed in a series of oral repeated dose toxicity studies in rats and dogs. A publication summarises the main findings from several unpublished company studies although limited details were reported on the test results (Hodge, 1964). These data were considered “not assignable” as the primary reports and description of raw data were not reported. However, the author seems to have reported the main findings.

STPP was administered for 1 month to groups of 5 male weanling (6-week old) rats at doses of 0.2, 2.0 and 10% in the diet (Hodge, 1964). One control group received the basal diet only, one additional control group received the basal diet supplemented with 10% Sodium chloride, and one control group received 5% orthophosphate. Growth reduction was observed at the high dose of 10%, and in the control group receiving basal diet with 10% sodium chloride. Enough calcium was added to the diet to ensure a “reasonably balanced” ratio of calcium to phosphorus (no further details). Growth was normal in rats receiving 2% sodium tripolyphosphate. No data were available on food consumption, clinical signs, or haematology. An increased relative kidney weight was observed at the highest dose of STPP and in the control group supplemented with NaCl. Histopathological examination showed tubular necrosis in the kidneys of rats treated at 10% sodium tripolyphosphate, and in the control group with 5% orthophosphate. Only inflammatory changes of the renal pelvis were observed at 2%, while normal kidneys were observed at 0.2%. Based on the renal effects, the NOEL was determined to be 0.2%. Assuming a 0.4 kg rat eats about 18 g of food per day, the NOEL for the 1-month diet study is therefore estimated to be 90 mg/kg/day for STPP. Furthermore, in this study, other groups of rats received similar doses of other inorganic condensed phosphates (sodium hexametaphosphate, sodium trimetaphosphate and sodium tetrametaphosphate), which produced similar effects, especially at 10%.

Sodium tripolyphosphate was further assessed in a 104-week oral repeated dose study in rats (Hodge, 1964). A preliminary assay was conducted with groups of 14 male rats, at doses of 0.2%, 2% and 10% STPP for 1 month. The effects described above for the previous study (growth retardation, increase in kidney weights, and tubular degeneration and necrosis of the kidneys) were again observed at the highest dose.

In the main 2-year study, males and females rats (50 animals per dose group and per sex) received 0.05, 0.5 and 5.0% of STPP in the diet. Mortality, food consumption, body weights were monitored. At the end of the treatment period, organ weights, haematology, urine analysis, bone analysis and histopathology were evaluated.

Growth retardation was observed in the high dose group in males (throughout the study period) and females (slight during the first year, then more obvious during the second year). High mortality was reported in males and females due to several epidemics during the study. The high dose group was more affected (up to 80% in females of the 5% dose during the second year of the study).

Concerns about potential altered calcium to phosphorus balance were addressed by conducting bone analysis. Femur analysis of the high dose group (5%) showed a slight increase in water content and slight decrease in organic matter as compared to the control group. No anomalies were observed at the bone radiography. The ash contents and ratios calcium to phosphorus were normal in both sexes of the high dose group.

The effects observed after repeated oral ingestion of high doses of STPP were anaemia observed after 1 year of treatment at 5% (decrease in red blood cells counts, haemoglobin values and haematocrits), and mainly renal effects. In the high dose group (5%), kidney

weights were increased in males, and relative liver and kidney weights were found increased in females. Histopathological examination showed enlargement of the kidney associated with tissue changes such as dilated convoluted tubules, hyaline casts, interstitial fibrosis between the dilated tubules, fibrotic glomeruli and intertubular calcification also in the group receiving the 5 % dose.

Based on the renal effects (nephrocalcinosis), the NOEL was estimated to be 0.5% for the 2-year repeated dose study in rats. Assuming a 0.4 kg rat eats about 18 g of food per day, the NOEL is estimated to be 225 mg/kg/day.

The effects on kidneys observed with STPP in the two-year study were consistent with those reported in other less documented studies, and for various other inorganic condensed phosphates such as sodium hexametaphosphate, sodium trimetaphosphate and sodium tetrametaphosphate (Hahn et al., 1958; Hahn, 1961; JECFA, 1982; TNO-BIBRA, 1993, Weiner et al., 2001). They are possibly related to the phosphate and calcium imbalance in the organism which can result from high intakes of phosphorus.

Following the review of available toxicity data on phosphates by an expert group commissioned by the World Health Organisation, the Maximum Tolerable Daily Intake of all phosphates was based on the lowest level of phosphates that produced nephrocalcinosis in the rat (1% phosphorus in the diet), and after extrapolations was estimated to be 70 mg/kg/day for man (when the food regimen contains nutritionally adequate amounts of calcium) in total phosphorus from all sources, including additives (JECFA, 1982). STPP is also an authorised food additive in Europe (E451(i)) (EC, 1995), as well as in the US (GRAS status) (FDA, 2001), provided that the diet contains nutritionally adequate amounts of calcium, and that the phosphate production complies with good manufacturing practices. However, the use of STPP as a food additive is relatively minor as compared with the use in household detergents.

No experimental data were available following repeated dermal exposure to STPP. One 6-month inhalation study in rats was identified in the literature, but the foreign publication was not available for assessment. No repeated studies were available via the dermal or inhalation routes. However, the oral route is considered appropriate for the risk assessment.

Conclusion

In a 2-year oral study in rats, STPP at high doses was found to cause growth retardation, some haematologic effects, and effects on the kidneys (mainly nephrocalcinosis). The NOEL was estimated to be around 225 mg/kg/day. Although limited documentation was available on that study, the effects reported were consistent with data obtained in several other studies using STPP as well as various inorganic condensed phosphates.

5.2.1.6 Genetic Toxicity

The available *in vitro* genotoxicity studies were not performed according to current guidelines and GLP. However, STPP was found not mutagenic in several reliable studies, including Ames tests in *S. typhimurium* and *E. coli*, chromosomal aberration test in CHL cells (Shimizu et al., 1985; Ishidate et al., 1984, 1988).

Pentasodium triphosphate (90% purity) was assessed in a modified Ames test at concentrations between 5 and up to 5000 µg/plate, with and without metabolic activation (Shimizu et al., 1985). The preincubation method was used in the presence of metabolic

activation. The bacterial strains used were *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538, and *Escherichia coli* WP2uvrA. The test was performed in duplicate, and appropriate positive and negative controls were used. No cytotoxic effects were observed. No increase in the number of revertants was observed, with or without S-9 mix.

No mutagenic activity was found in a reverse mutation assay performed in *Salmonella typhimurium* strains TA92, TA94, TA98, TA100, TA1535, and TA1537 with STPP (84.1% purity) at concentrations up to 10 mg/plate (Ishidate et al. 1984). Limited documentation was available on methodology and test results (no positive controls, no details on doses tested, no indication of cytotoxicity). However, test results support the absence of mutagenic activity of sodium tripolyphosphate.

STPP (84.1% purity) was assessed for chromosomal aberrations in Chinese Hamster fibroblasts cell line (CHL) (Ishidate et al. 1984). Cells were treated at 3 different doses for 24 or 48 hours, without metabolic activation. The maximum dose tested was determined in a preliminary assay not reported in the publication. The value of the maximum concentration tested (determined in a preliminary assay) was not legible in the publication (missing value in the result table). One hundred well-spread metaphases were analysed for incidence of polyploid cells, structural aberrations (chromatid or chromosome gaps, breaks, exchanges, ring formations, fragmentations and others). No significant effects were observed. Reporting of the methodology and results was rather limited. No metabolic activation was used. There was no information on cytotoxicity, and whether the test concentrations were optimal. No positive controls were included.

These negative results were further supported by another publication reporting the results of a chromosomal aberration assay in Chinese Hamster fibroblasts cell line (CHL) (Ishidate et al. 1988). STPP was tested at a maximum concentration of 500 µg/ml (1.4 mM) for a treatment time of 48 hours. No other doses were mentioned. The vehicle was not indicated. No metabolic activation was used. No structural aberrations were reported. Limited documentation was available on test conditions and results.

A cytogenetic study in human lung cells, as well as an *in vivo* cytogenetic study in rat bone marrow cells, and a dominant lethal study in rats were also reported as negative (Litton Bionetics Inc., 1974; citation in Weiner et al., 2001, and JECFA, 1982). Limited information was available on these latter studies described in secondary literature. However, the negative results support the lack of evidence for genetic toxicity for STPP *in vivo*.

Conclusion

Although limited documentation was generally available on these assays reported in the literature, altogether the negative results obtained in various assays support the lack of evidence for genetic toxicity for STPP *in vitro* and *in vivo*.

5.2.1.7 Carcinogenicity

In a chronic oral toxicity study in rats, males and females (50 animals of each sex per dose group) were fed 0, 0.05, 0.5 and 5.0 % STPP (5% corresponds to approx. 1.5 g/kg bw/day) in the diet for 104 weeks. Results of the study were summarised in a publication where only the main findings were described (Hodge, 1964) (see “repeated dose toxicity” above).

Animals of the highest dose group exhibited retarded growth. Anaemia and renal calcification were observed in males. No significant toxic effect was observed at the lower doses of 0.05% (15 mg/kg/day), or at 0.5%. High mortality was observed during the 2nd year in the group treated at the highest dose (especially in females, with up to 80% mortality), and was mainly due to respiratory infections and pericarditis-peritonitis. Increase in kidney weight was observed in males treated at 5%, as well as histopathological changes (chronic tubular nephropathy) distinct from the chronic lesions present in old rats. No toxic effects were observed at the lowest dose of 0.05%. This study showed no indication that STPP could be carcinogenic. No significant increase in tumour incidence was observed.

Similarly, no increase in tumour incidence was observed with other inorganic condensed phosphates (e.g., sodium hexametaphosphate and sodium trimetaphosphate) (Hodge, 1964; Weiner et al., 2001; TNO-BIBRA, 1993).

Conclusion

The long-term study that was available was not performed according to GLP or current guidelines for carcinogenicity assays, and there was a high level of mortality in the high dose group due to repeated infections, which weakens the reliability of this study. However, no significant increase in tumour incidence was observed in this study to indicate that STPP could be carcinogenic. In addition, there are also no particular concern with regard to genotoxic activity, as reported in the previous section.

5.2.1.8 Toxicity to reproduction

A 3-generation study in rats was available in the literature (Hodge et al., 1964). At a dose of 0.5% in the food, STPP showed no evidence of significant alteration of fertility, nor on the litter size, nor on growth and survival of offspring. A slight increase in kidney weights was observed, but was not statistically significant. The macroscopic and microscopic appearances of major organs in the 3rd generation were reported to be comparable in control and treated groups. These results were presented as a summary of unpublished reports from a detergent company, and limited documentation was available. However, any significant effects seem to have been reported by the author. The results provided support the assumption that there is no concern with regard to effects of STPP on reproduction.

Similar data were reported with other condensed inorganic phosphates (Hodge, 1964). No effects on fertility, litter size, growth or survival of offspring were observed in 3-generation studies conducted in rats maintained on diets containing either 0.05% sodium trimetaphosphate or 0.5% sodium hexametaphosphate. No abnormality was observed in the organ weights of the third generation rats at weaning, and at histopathological examination of tissues. Very limited information was available on these data. In addition, no reproductive effects were reported for monovalent orthophosphoric acid (Weiner et al. 2001).

Conclusion

Studies reported briefly in the literature indicated no evidence of reproductive effects for STPP and several other inorganic phosphates. These results are also supported by data on two other inorganic condensed phosphates and monovalent orthophosphoric acid, which tend to support the absence of reproductive effects of STPP, and inorganic phosphates in general.

5.2.1.9 Developmental Toxicity/Teratogenicity

Unpublished company reports submitted to FDA and reviewed by the World Health Organisation JECFA committee showed no maternal toxicity and no teratogenic effects in developmental studies after oral administration of STPP at dose levels up to 170 mg/kg/d in rats, 238 mg/kg/d in mice, 141 mg/kg/d in hamsters, or 250 mg/kg/d in rabbits (Food Drug Res. Lab. 1973a, 1973b; JECFA, 1982; Weiner et al., 2001). The original reports were not available for assessment, and limited documentation was available on the test results in the JECFA evaluation report (1982) and in the review from Weiner et al (2001).

In these studies, pregnant females received STPP (anhydrous) during gestation period by oral intubation. Control groups received the vehicle only (water). At the end of gestation period, all dams were subjected to caesarean section and the number of implantation sites, resorption sites, as well as live and dead foetuses were recorded. The body weights of the live pups were taken. The urogenital tract level of dams was examined for abdominal abnormalities. All foetuses were examined for the presence of external congenital abnormalities. One-third of the foetuses were examined for visceral abnormalities and the remaining two-third were examined for skeletal abnormalities. No maternal toxicity or teratogenic effects were observed at up to the maximum dose levels tested in each species. The NOEL for maternal and foetal toxicity corresponded to the maximum dose tested. However, the validity of these data cannot be fully assessed as no information was available on the dose selection, and the maximum tolerated dose was probably not reached in these assays. Similar results were reported with other condensed inorganic phosphates (Weiner et al., 2001).

Table 10 : Summary of teratogenicity studies with sodium tripolyphosphate

	animal / group	Dose (mg/kg bw)	Treatment period (gestation day)	End of gestation	Result (NOEL)	Ref.
Mouse	24	2.4, 11, 52, 238	6-16	Day 17	238 mg/kg	(1)
Rat	24	1.7, 8, 37, 170	6-15	Day 20	170 mg/kg	(1)
Hamster	22-25	1.41, 6.5, 30, 141	6-10	Day 14	141 mg/kg	(1)
rabbit	20-22	2.5, 11.6, 54, 250	6-18	Day 29	250 mg/kg	(2)

References: (1) Food Drug Res. Lab, 1973a; (2) Food Drug Res. Lab, 1973b

Conclusion

The information available did not show evidence of teratogenic effects in mice, rats, hamsters or rabbits following exposure to STPP.

5.2.1.10 Additional data

Toxicokinetics, metabolism

Phosphates and Polyphosphates toxicity data and metabolism have been reviewed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA, 1982). Various studies tend to indicate that polyphosphates are not absorbed as such in the intestinal tract, but they can be hydrolysed *in vivo* by enzymes with the formation of monophosphates, mainly orthophosphate and possibly pyrophosphate, which are then absorbed (Gosselin et al., 1952; Ebel, 1958; Hahn, 1961; JECFA, 1982). This is further supported by the fact that systemic effects of polyphosphates are very similar to those of orthophosphates (Hahn, 1961; JECFA, 1982). It was estimated that approximately two-thirds of ingested phosphates is absorbed from the gastro-intestinal tract.

No data have been identified with regard to dermal absorption properties. It is generally considered that the percutaneous absorption of salts or ionic substances is limited (Schaeffer and Redelmeier, 1996).

5.2.1.11 Experience with human exposure

There have been only a few published case reports of health effects or discomfort associated with potential exposure to STPP by skin contact or inhalation. One isolated case of an asthmatic-like reaction was described in an atopic asthmatic patient following airborne exposures to what was estimated (using exposure modelling) to be significant concentrations of STPP and volatile organic compounds caused by a carpet-cleaning job (Lynch, 2000). Asthmatic-like symptoms can occur in asthmatic persons who are more susceptible to irritant and volatile organic compounds than non-asthmatics, and show greater bronchial hyper-responsiveness to irritant exposure than non-asthmatics. Estimation of the exposure to STPP using an exposure model indicated possible exposure at, or above, the recommended short-term exposure limit for workers. However, there was no evidence that the observed effects were attributable to an immunologic response to a particular component present in the products used (STPP or volatile organic compound).

One publication reported one single positive sensitisation response to STPP after a single patch test (48-hour occlusive application) at a concentration of 2% in petrolatum in a study performed on 190 workers of the ceramics industry. Part of the panel had previous history of skin problems (23.1%), or dermatitis (11.5%). No reactions were observed in a control group of 100 healthy volunteers exposed to a single 2% patch application (Motolese et al., 1993).

In addition, indirect contact with detergent residues on clothes was found not to be a cause of cutaneous reactions (Matthies et al., 1990). After 25 washes with phosphate-free or phosphate-containing laundry detergents (nature of phosphate not indicated), cotton and polyester fabrics were used for occlusive patch testing for 48 hours on seborrheic and seborrheic volunteers (20 of each type). No skin reactions were observed in all cases.

Allergies, rashes, sinus problems and sneezing were reportedly associated with dust exposures of workers who packaged various compounds, including STPP (publication abstract, Lenhart, 1999).

To the best of our knowledge, no cases of poisoning or toxicity have been reported in the literature for sodium tripolyphosphate. Accidental ingestion of a large quantity of detergent

liquids is usually unlikely because of the addition of bitter agent to the products to discourage children from drinking them. However, in some cases, determined adult can overcome the bitter taste and consume toxic quantities. One publication reported the case of a 30-year-old woman who ingested deliberately an unknown amount of a mixture of domestic laundry cleaning and fabric conditioner containing more than 30% sodium phosphate (no further details, possibly sodium orthophosphate), phosphonate, anionic and nonionic surfactants (each at less than 5%) (Vincent and Sheikh, 1998). The amount of product ingested was not known. The woman developed the clinical signs of phosphate signs of hypocalcaemia leading to ventilatory failure because of respiratory muscle spasm, abdominal pain, agitation, trismus. Biochemical investigations showed an increase in serum phosphate and sodium, decrease in serum magnesium and calcium. The metabolic disturbance resolved after supportive treatment and 16 hours of controlled ventilation. There was no similar case identified of an accidental ingestion with a sodium tripolyphosphate-containing detergent.

5.2.2 Identification of critical endpoints

5.2.2.1 Summary of toxicological endpoints

Experimental data showed a low acute toxicity potential for STPP by the oral or dermal routes with LD50 values greater than 2000 mg/kg by either routes. The maximum attainable concentration of STPP that could be technically generated showed no significant clinical signs except reactions consistent with exposure to an irritant dust.

Because of potential direct skin and eye contact with detergents, as powder or liquid formulation, ocular effects, and skin irritation or sensitisation must be addressed. However, STPP was found at most slightly irritating to the intact skin or to the eyes when tested neat, or in aqueous solutions.

In the animal database, ocular effects were usually limited to conjunctival reactions following exposure to STPP as a powder, and this substance is not considered irritating to the eyes. Solutions at 1% or 10% STPP also showed no signs of irritation. Therefore, STPP is not likely to contribute significantly to the overall eye irritation hazard of a formulated detergent. Furthermore, no sensitisation reactions were observed following cutaneous exposures to formulations containing STPP in animals (Büehler test), and in human volunteers (repeated insult patch tests).

There are also no reports of skin sensitisation occurrence associated with STPP exposure in consumers. An occupational exposure study in the enamelling industry using a unique patch testing showed no reaction in a panel of 100 healthy volunteers and one reaction observed in an enameller among a panel of 190 industry workers who could have been previously exposed to STPP. Furthermore, no sensitisation effects have been reported for related phosphate derivatives, such as phosphoric acid and ammonium polyphosphate.

Repeated dose toxicity studies by the oral route showed that STPP induced retarded growth, anaemia and renal calcification at 2% and higher. In a 2-year study, no toxic effect was observed at the doses of 0.05% (15 mg/kg/day) and 0.5%. From this study, a NOEL could be estimated at 0.5 % [i.e. 225 mg/kg/d assuming a 0.4 kg rat eats 18g food/d], based on the dose at which no histopathological effects were observed on kidneys. Similar effects were observed with all types of inorganic condensed phosphates.

These results are consistent with the use of STPP and other phosphate derivatives as food additives, and GRAS (Generally Recognised As Safe) status in the United States (FDA, 2001). STPP is also an authorised food additive in Europe, E451(i) (EC, 1995). However, the use of STPP as a food additive is considered minor as compared with its use in household detergents.

Based on literature data, STPP is not considered to be mutagenic or genotoxic. The oral long-term toxicity study did not show any evidence of a carcinogenic potential of sodium tripolyphosphate.

No significant adverse effects were reported in a 3-generation reproductive toxicity study in rats.

Teratogenicity studies showed no maternal toxicity and no fetal toxicity or teratogenic effects at up to the highest dose tested in four different species, rats (170 mg/kg), mice (238 mg/kg), hamsters (141 mg/kg) and rabbits (250 mg/kg).

The available experimental data indicate that acute and local effects are not a primary cause of concern, although overexposure can occur by accidental ingestion of household cleaning products, and accidental spillage can expose the eyes.

The repeated dermal exposure is to be considered as the main exposure route for consumers using household detergents. However, the systemic effects resulting from a long-term oral exposure were considered relevant for the assessment and were then taken into account.

5.2.3 Determination of NOAEL

The life-time feeding study in rats was considered the most relevant to STPP exposure in consumers, because of potential systemic exposure through repeated daily use of detergents containing sodium tripolyphosphate.

A NOEL of 225 mg/kg/day from the 2-year oral toxicity study in rats was considered for the risk assessment.

5.3 Risk Assessment

5.3.1 Margin of exposure calculation

The Margin of Exposure (MOE) is the ratio of the No Observed (Adverse) Effect Level and the predicted exposure level or systemic estimated dose (SED) as calculated above in section 5.1.3. From the available animal studies, the 2-year life-time feeding study in rats provided a NOEL = 225 mg/kg/d.

Because ionic substances are considered to be less easily absorbed than non-ionic compounds (Schaeffer and Redelmeier, 1996), as a worst case assumption a percutaneous absorption of 1% in 24 hour exposure time was used in the assessment of the systemic exposure by dermal route. This estimation is compared to the NOEL value obtained in a repeated oral dose study.

Contact from hand washing laundry with solutions which contain STPP

$$\begin{aligned} \text{MOE}_{\text{direct skin}} &= \text{systemic oral NOEL/estimated systemic dose} \\ \text{MOE}_{\text{direct skin}} &= (225\ 000\ \mu\text{g/kg/d}) / (0.3\ \mu\text{g/kg/d}) = \mathbf{750\ 000} \end{aligned}$$

The systemic dose was estimated from the worst case scenario, using the highest use concentration and use frequency. The other products (liquid detergent or laundry tablets) would result in a lower exposure, and therefore in a larger margin of exposure.

Contact from pre-treatment of clothes with product containing sodium tripolyphosphate

$$\begin{aligned} \text{MOE}_{\text{direct skin}} &= \text{systemic oral NOEL/estimated systemic dose} \\ \text{MOE}_{\text{direct skin}} &= (225\ 000\ \mu\text{g/kg/d}) / (7.5\ \mu\text{g/kg/d}) = \mathbf{30\ 000} \end{aligned}$$

The systemic dose was estimated from the worst case scenario, using the highest use concentration and use frequency. The other products (liquid detergent or laundry tablets) would result in a lower exposure, and therefore in a larger margin of exposure.

Contact from surface cleaning with product containing STPP

$$\begin{aligned} \text{MOE}_{\text{direct skin}} &= \text{systemic oral NOEL/estimated systemic dose} \\ \text{MOE}_{\text{direct skin}} &= (225\ 000\ \mu\text{g/kg/d}) / (0.1\ \mu\text{g/kg/d}) = \mathbf{2\ 250\ 000} \end{aligned}$$

Indirect skin contact via wearing clothes

$$\begin{aligned} \text{MOE}_{\text{indirect skin}} &= \text{systemic oral NOEL/estimated systemic dose} \\ \text{MOE}_{\text{indirect skin}} &= (225\ 000\ \mu\text{g/kg/d}) / (14\ \mu\text{g/kg/d}) = \mathbf{16\ 070} \end{aligned}$$

Oral exposure

The total estimated exposure to STPP via the environment or from residues left on eating utensils and dishes was 11 $\mu\text{g/kg/d}$.

$$\begin{aligned} \text{MOE}_{\text{direct oral}} &= \text{systemic oral NOEL/estimated systemic dose} \\ \text{MOE}_{\text{direct oral}} &= (225\ 000\ \mu\text{g/kg/d}) / (11\ \mu\text{g/kg/d}) = \mathbf{20\ 450} \end{aligned}$$

Inhalation

The total estimated exposure to STPP by inhalation while pouring detergent powder into a machine, or inhaling aerosols generated by spray refreshers was below 0.1 $\mu\text{g/kg/d}$.

$$\text{MOE}_{\text{inhalation}} = \text{systemic oral NOEL/estimated systemic dose}$$

$$\text{MOE}_{\text{inhalation}} = (225\,000 \mu\text{g/kg/d}) / (0.1 \mu\text{g/kg/d}) = \mathbf{2\,250\,000}$$

Total consumer exposure

The integrated consumer exposure to STPP via all routes results in an estimated total body burden of $21.9 + 11 + 0.1 \mu\text{g/kg/d} = 33 \mu\text{g/kg bw/day}$.

Comparison of the total predicted consumer exposure to STPP with the systemic NOEL (225 mg/kg/d) results in an estimated Margin of Exposure of approximately 6 800.

Overexposure and accidental contact with eyes

The experimental acute oral toxicity for STPP was found greater than 2000 mg/kg in rats. The uptake of STPP must be high to reach acute lethal effects. In two studies, no lethal effects were observed at 2000 and 2150 mg/kg in rats. Clinical signs included altered respiration and depression. This would correspond to the ingestion of 120 g by an adult of 60 kg, or 20g by a 10-kg child, and an even higher amount of the detergent containing up to 60% sodium tripolyphosphate. No fatal cases of poisoning were reported with STPP-containing detergents, although one case of intentional ingestion of laundry detergent by a determined adult was described in the literature. The amount of detergent swallowed was not known. Symptoms were those of phosphate poisoning (the formulation contained more than 30% sodium phosphate), i.e. hypocalcaemia and ventilatory failure which were overcome successfully by supportive treatment. This is an unlikely case in young infants because the amount ingested accidentally by children is generally limited by the taste of the detergent. It seems that child poisoning cases are not usually severe, except in case of massive ingestion or bronchial aspiration of foam (Petersen, 1989; Repetto, 1996; Herrington et al., 1998). Published data indicate that most cases of accidental ingestion of laundry or dishwashing products by young children involve small amounts of product (1 teaspoon or less) (Petersen, 1989).

Experimental data show that STPP is only slightly irritating to the skin and eyes. Some cutaneous reactions could however be observed on injured skin. Based on these results, STPP is not likely to contribute to the irritation potential of the detergent formulations.

5.3.2 Risk characterisation

Skin contact, inhalation and oral ingestion scenarios were assessed for human exposure to STPP in detergents, comprising laundry and automatic dishwashing detergents, as well as hard-surface and toilet cleaners.

The Margin of exposure for the combined estimated systemic exposures is 6 800. This margin takes into account uncertainties and variability associated with the hazards database, such as inter- and intra-species variability, as well as extrapolation.

Number of worst case assumptions were made for the estimation of exposure. Maximal use frequency and use quantities were used in the calculations, and in the absence of specific data, default values were used in the estimation of exposure. Therefore this margin of exposure does not raise any particular safety concerns with regard to systemic or local effects of STPP for use in consumer detergent products.

5.4 Discussion and Conclusions

Experimental data showed that STPP has a low acute toxicity by the oral and dermal routes (LD50 > 2000 mg/kg by either routes). By oral ingestion, STPP is reported to be bioavailable

after hydrolysis into sodium orthophosphate in the intestinal tract. At massive concentrations, e.g. in case of accidental or intentional ingestion, it may increase plasmatic content in phosphorus and a decrease in calcium content.

Limited amount of dust could be generated from sodium tripolyphosphate, and no toxicity was found in an acute inhalation assay. The size of the particles generated by using a spray, or from detergent dust is not expected to be in the respirable range. Furthermore, it is estimated that very low levels of STPP dust should be generated from laundry powder detergent or from spray aerosols, and would result in a limited potential irritation on the respiratory tract.

Because of potential direct skin contact with detergents, as powder or liquid formulation, skin irritation and sensitisation were taken into consideration in the risk assessment. According to the database, slight or no irritating effects were observed in animals after dermal application on intact skin or following ocular exposure, although some effects could be observed on injured skin. STPP is therefore not expected to contribute to the irritating potential of detergents used by the consumer. In addition, indirect contact with detergent residues on clothes was found not to be a cause of cutaneous reactions (Matthies et al., 1990).

Sensitisation potential was not assessed with STPP as such, but experimental data in animals and results of Repeated Insult Patch Tests in human volunteers with various formulations containing STPP showed no evidence of sensitisation potential.

Furthermore, to the best of our knowledge, there are no reported cases of skin contact sensitisation related to STPP exposure in consumer detergents. Direct skin exposure to STPP was estimated by various scenarios and was found relatively low. Furthermore, the dermal bioavailability for ionic substances is assumed to be limited.

Based on literature data, STPP is not considered to be mutagenic or genotoxic. The oral long-term toxicity study did not show any evidence of a carcinogenic potential of STPP in a chronic study in rats. There was no evidence of adverse reproductive or developmental effects in various species at the highest doses tested.

Repeated dose toxicity studies by the oral route showed that STPP induced retarded growth, anaemia and renal calcification. In a 2-year study, no toxic effect was observed at the doses of up to 0.5%, which was used to estimate a systemic NOEL of 225 mg/kg/day.

The consumer aggregate exposure to STPP in household cleaning products, from direct and indirect contact by oral, dermal or inhalation routes results in a total body burden of 33 µg/kg bw/day. This value corresponds to approximately 8.4 µg Phosphorus/kg bw/day, which is far below the Maximum Tolerable Daily intake (MTDI) for total phosphorus in the food, established by WHO at 70 mg/kg bw (JECFA, 1982). Exposure to STPP through the use of detergents is therefore minor when compared to total intake of phosphorus as a nutrient in the diet (either from food additives, or from natural sources). A recent survey conducted in Ireland between 1997 and 1999 in people aged 18 to 64 reported a daily intake of 1645 mg (± 463) for males, and 1161 mg (± 318) for females (Kiely, 2001). Based on these figures, and a body weight of 70 kg for men and 60 kg for women, the daily intake of total phosphorus from all dietary sources is equivalent to approximately 24 mg/kg in a European country, i.e. 34% of the Maximum Tolerable Daily intake recommended by WHO committee.

Comparison of the total estimated systemic exposure to STPP through the use of detergents (33 µg/kg/day) to the No Effect Level estimated in animals (225 mg/kg/day) results in a margin of exposure of approximately 6 800, which is large enough to conclude that STPP is of low concern for the consumer use in household detergents.

6 References

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