THIS DOCUMENT HAS BEEN PREPARED ACCORDING TO THE PROVISIONS OF ARTICLE 136(3) “TRANSITIONAL MEASURES REGARDING EXISTING SUBSTANCES” OF REACH (REGULATION (EC) 1907/2006). IT IS NOT A PROPOSAL FOR A RESTRICTION ALTHOUGH THE FORMAT IS THE SAME

ANNEX XV TRANSITIONNAL REPORT

SUBMITTED BY: FRANCE

DATE: 20.11.2008

SUBSTANCE NAME: **TNPP (tris(nonylphenyl) phosphite)**

CAS NUMBER: 26523-78-4
EC NUMBER: 247-759-6

A. SUMMARY

It has been concluded from the risk assessment of TNPP that there is a concern due to skin sensitisation upon dermal contact during manufacture of the substance, manufacture of products containing TNPP and use of preparations containing TNPP.
Therefore a Risk Reduction Strategy with respect to worker has been developed and agreed at the last RRSM in april 2008. Classification of TNPP as a sensitizer was finalised in the Commission working group on the Classification and Labelling of Dangerous Substances in November 2005. As a result of its classification as hazardous substance, TNPP is subject to general regulations concerning its supply and handling and to the legislation for workers' protection currently in force at Community level. These regulations are generally considered to give an adequate framework to limit the risks of the substance to the extent needed and shall apply. Therefore, no further risk reduction measures are recommended.
No risk was observed for the consumer.
Following TCNES I' 08 the meeting confirmed the need of further testing for the aquatic compartment and a chronic Daphnia study with TNPP was requested. Recently, industry requested additional time to submit the remaining information requirements (Commission Regulation (EC) No 466/2008 of 28 May 2008). Results are expected for the end of 2008.

B. INFORMATION ON HAZARD AND RISK

B.1 Identity of the substance(s) and physical and chemical properties

B.1.1 Name and other identifiers of the substance(s)

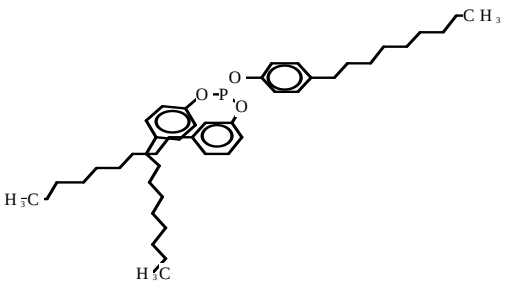
CAS No: 26523-78-4

EINECS No: 247-759-6

IUPAC Name: Phenol, nonyl-, phosphite (3:1)

Molecular formula: $C_{45}H_{69}O_3P$

Structural Formula:



Molecular weight: 689 $g.mol^{-1}$

Synonyms and tradenames: Alkanox TNPP, Lowinox TNPP, Irgafos TNPP, Tris(monononylphenyl)phosphite, Tri(nonylphenyl)phosphite,

Weston 399, Weston TNPP, Irgastab CH 55, Naugard TNPP, Polygard, Polygard HR, Polygard LC, TNPP, Trisnonylphenylphosphit.

In this assessment, the name Tris(nonylphenyl)phosphite (TNPP) will be used for the substance as this is the most common name.

B.1.2 Composition of the substance(s)

The purity of TNPP is reported as ca. 95 – 100% w/w.

The following impurities may be found in TNPP :

- Nonylphenol (CAS 25154-52-3) < 5% w/w,
- Phenol (CAS 108-95-2) < 1% w/w,
- Di(nonylphenyl)phenylphosphite (CAS 25417-08-7) 0.05% w/w,
- Chlorine (CAS 7782-50-5) 0.005% w/w.

B.1.3 Physico-chemical properties

For more details, refer to 1.3 of the RAR in annex.

Table B.0.1: Physical and chemical properties of the TNPP

Property	Value	Comments
Physical state at ntp	Viscous liquid	
Molecular weight	689 $g.mol^{-1}$	
Melting Point	6°C ± 3°C	Instead of a melting point, a pour point (more appropriate to viscous liquids) was determined
Boiling Point	322°C	Degradation
Relative density	0.98 $g.cm^{-3}$	
Vapour pressure	0.058 Pa at 25°C	extrapolated from results obtained by isoteniscope (method ASTM D2879)
Partition coefficient	Log Kow = 21.6 Log Kow = 8 (EUSES)	Calculated with software ACD/LogP DB
Water solubility	<0.6 $mg.L^{-1}$	A saturated solution was not obtained and the water solubility result corresponds to the detection limit of the analytical method.
Flash point	207°C	Pensky Martin apparatus (closed cup)
Autoflammability	440°C	Setchkin method
Oxidising properties	No oxidising property	
Henry's law constant	66.6 $Pa.m^3.mol^{-1}$	TGD calculation

B.1.4 Justification for grouping

No grouping proposed

B.2 Manufacture and uses

For more details, refer to chapter 2 of the RAR joined in annex.

B.2.1 Manufacture and import of a substance

TNPP is produced all over the world: Unites States, Europe, India, Korea, Russia, China, etc. (Chemical Information Services, 2002). Three facilities are currently producing TNPP in Europe. On the other hand, the major source of TNPP to Europe is from the United States.

The manufacturing processes used to produce TNPP are reasonably similar in the various plants in the US and Europe. Figure 0-1 is providing an overview of a typical production process.

TNPP production is carried out in a closed system where nonylphenol (NP) and phosphorus trichloride (PCl_3) are added to the reactor (ca. 3 :1) and held at greater than 110°C to ensure all the PCl_3 is consumed. The HCl by-product is vented to an absorber. The HCL by-product can be filtered and stored for sale or use in other processes. Excess nonylphenol is stripped from the product. The stripped nonylphenol can be recycled. The product TNPP in the reactor after stripping is pumped to a storage tank for packaging and sale. The product may be packaged into drums, isotaners, rail cars, or tank trunks.

Environmental release and exposure

The process is fully automated (computer controlled) in a closed system. The reactor is operated under 3-5 lbs (1.4 – 2.3 kg) of pressure. The vacuum pump vent is the only potential process release to the atmosphere, and it is passed through a carbon filter. The storage tank is kept under nitrogen preventing release to the atmosphere. Nitrogen is also used during transfer and packaging.

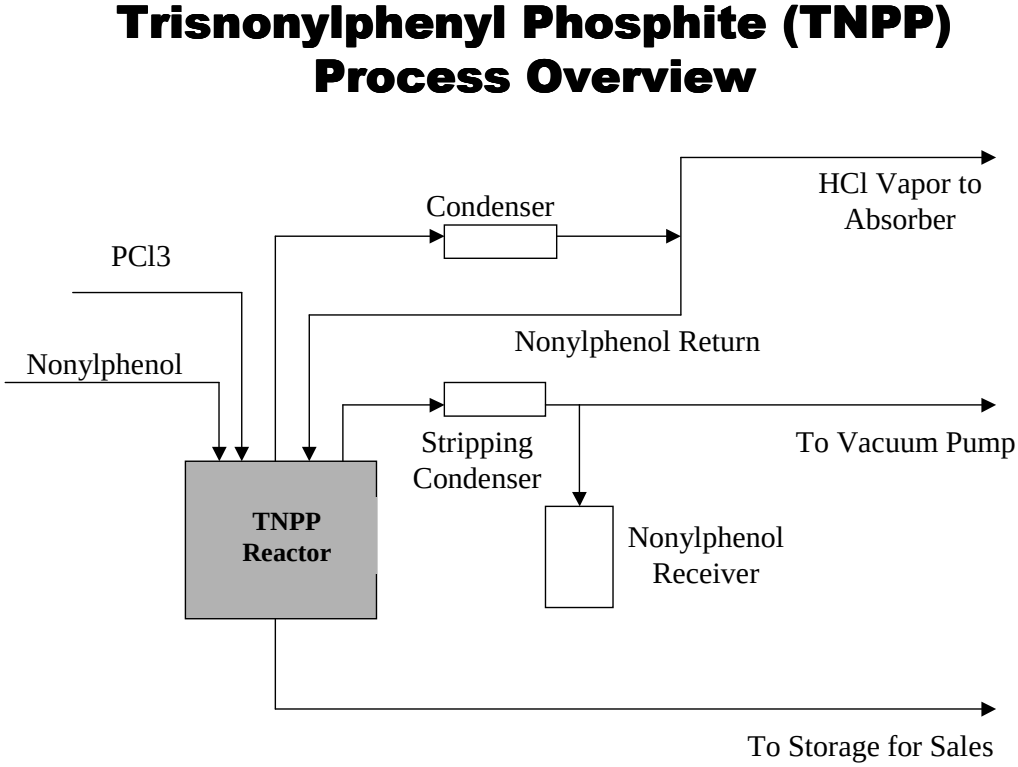


Figure 0-1: Process overview of tris(nonylphenyl)phosphite (TNPP) production

Production capacity

European and North American TNPP producers are organised under the Alkylphenols and Ethoxylates Research Council (APERC), a not-for-profit trade association, whose members have commercial interest in nonylphenol, octylphenol, and derivatives produced from these compounds. Information on production and imports of TNPP in Europe were provided by APERC TNPP Consortium. Hardly any individual volume was provided for each producer/importer.

Three facilities are currently producing TNPP in Europe. A fourth facility ceased TNPP production in 2001. Between 1990 and 1997, the production + import volumes were around 5,000 – 10,000 t/year.

Information is available on the combined estimate of TNPP produced within Europe and imported into Europe over the last three years:

- 1999 – approximately 5,565 tonnes
- 2000 – approximately 5,700 tonnes
- 2001 – approximately 6,800 tonnes

As this information is provided by the APERC TNPP Consortium, it cannot be excluded that these volumes do not take into account shipments of product from producers in other parts of the world than Europe and North America. However, according to the APERC TNPP Consortium, the quantity of TNPP from non-TNPP Consortium companies are not expected to be significant.

European production plants have also reported their production volumes for the year 2001. Imported volume for the same year is also available. Consequently, a total volume in Europe of 8,000 t. calculated with all 2001 data will be used in this report.

B.2.2 Uses

TNPP is used as a stabiliser in the processing of various plastic and rubber products. They are used with hindered phenolic antioxidants in plastic food packaging. In the stabilisation process, TNPP is gradually oxidised and nonylphenol is released (Building Research Establishment Ltd., 2001).

TNPP is also used as a secondary antioxidant in polymer formulations (Ullmann, 1985).

About 25 to 35 facilities are processing TNPP in Europe. Their consumption ranges from a few tonnes to over 400 tonnes/year.

An estimate of the breakdown of TNPP uses was developed based on an informal survey of North American and European manufacturers. Quantitative breakdown of TNPP uses are given in Table 2.1. The information pertains to sales of TNPP in 1999. It is expected that the breakdown of uses from the 1999 sales statistics is typical for the current year. Corresponding volumes are calculated using the total tonnage of 8,000 t.

Table B.0.2.1: Typical quantitative breakdown of TNPP Uses

	Percentage of tonnage	Volume (tonnes)	Industrial Category / Use Category
Polyvinylchloride (PVC) film	35%	2,800	IC 11 / UC 49
Polyolefins linear low density polyethylene (LLDPE)	15%	1,200	IC 11 / UC 49
High density polyethylene (HDPE)	10%	800	IC 11 / UC 49
Rubber	37%	2,960	IC 11 / UC 49
Other/Unknown	3%	240	IC 55 / UC 0
TOTAL	100%	8,000	

In the SPIN Database (Substances in Preparations in Nordic Countries), the following industrial uses are described:

Table B.0.2.2: Industrial uses of TNPP in the Nordic Countries (in Tonnes)

	1999[1]	2000[2]	2001[3]
Manufacture of chemicals and chemical products	156	27	< 0.1
Manufacture of rubber and plastic products	38	105	n. i.
Manufacture of furniture; manufacturing n.e.c.	n. i.	0.4	0.1
Manufacture of fabricated metal products, except machinery and equipment	n. i.	0.2	0.1
Construction	n. i.	0.2	0.1
Manufacture of wood and products of wood and cork, except	< 0.1	< 0.1	0.1

	1999[1]	2000[2]	2001[3]
furniture; manufacture of articles of straw and plaiting materials			
Total	194	132.8	0.4

n. i.: not indicated

[1]: Information was available for Sweden only

[2]: Information was available for Sweden, Denmark and Norway

[3]: Information was available for Denmark and Norway.

TNPP is also mentioned in the following industrial categories: publishing, printing and reproduction of recorded media / sale, maintenance and repair of motor vehicles and motorcycles; retail sale of automotive fuel / manufacture of other transport equipment n.e.c. However, the volumes used in such industries could be considered as negligible (> 0.1 t/y in each country).

Besides, the following use pattern is described in the SPIN database:

Table B.0.2.3: Use pattern of TNPP in the Nordic Countries (in Tonnes)

	1999[1]	2000[2]	2001[3]
Stabilizers	118	120	n.i.
Intermediates	-	1	n. i.
Others	1	1	n. i.
Adhesives, binding agents	n. i.	0.5	< 0.1
Paints, lacquers and varnishes	< 0.1	0.3	< 0.1
Fillers	< 0.1	> 0.1	0.2
Total	119	122.8	0.2

n.i.: not indicated

[1]: Information was available for Sweden only

[2]: Information was available for Sweden, Denmark and Norway

[3]: Information was available for Denmark and Norway.

TNPP is also mentioned in the following use categories: lubricants and additives / reprographic agents. However, the volumes used in such applications could be considered as negligible (> 0.1 t/y in each country).

From these tables, it could be stated that TNPP is mainly used as a stabiliser for the manufacture of rubbers and plastic products. The breakdown of TNPP uses described in Table will be used in this risk assessment.

Industrial use

Formulation and processing steps are necessary to manufacture plastic and rubber products. Formulation could be defined as the stage where TNPP is combined in a process of blending and mixing into a polymer or into another material while during the processing step, the TNPP containing material is formed. It is not known to what extent formulation and processing may occur at the same site. In the rubber industry, these two steps can often

not be viewed separately (E.C., 2003, Emission Scenario Document for IC 15: others: rubber industry).

Therefore, as a worst assumption, formulation and processing stages will be assumed to occur at one site for every uses.

Without any specific information, it could be considered that TNPP is used for polymer processing, in the sub-category "processing of thermoplastics" as a processing aid. This categorisation will be used in the risk assessment for the determination of the default releases factors.

Besides, for plastic and rubber products, stages of private use and recovery may be considered. However, no specific information is available on the possible releases of TNPP during these stages.

All calculations will be performed using EUSES default parameters and, when available, emission factors issued from the emission scenario document on plastics additives (OECD, 2004).

Production of Polyvinylchloride (PVC) film

PVC containing TNPP may be used in many products like shower curtains, floorings and wall coverings.

Production of Polyolefins linear low density polyethylene (LLDPE)

LLDPE films containing TNPP are used for the manufacture of bags and food packaging. Many national regulations are covering the use of TNPP in food contact materials (Table B.2.2.3

Table B.2.2.3: Global food contact regulations specific to TNPP

Country	Regulation
USA	Food and Drug Administration (FDA) – 21 CFR Part 178.2010
Japan	Self-restrictive Requirements on Food-Contact Articles Japan, Hygienic Olefin and Styrene Plastics Association (JHOSPA) (March 1996), Section A4-2, maximum 1.2%
European Union	Plastics Directive 2002/72/EC, pm/ref. No. 74400, specific migration limit 30 mg/kg
Germany	BfR Recommendation VI, maximum 2.0% total of all stabilisers BGA: maximum 6% in plastics
Netherlands	Food Packaging and Utensils Decree of 01.10.1979 as amended Chapter 1
France	Brochure 1227 (Avril 1990) maximum 1.0%
Italy	Min. Decree of 21.03.1973 maximum 0.3% Min. Decree of 0.04.1985
Spain	Royal Decree 125/1982 of 30.04.1982 Resolution of 4.11.1982
Belgium	Royal Decree of 11.05.1992, specific migration limit 30 mg/kg
United Kingdom	BIBRA/BBF Code of Practice (1991) Rec. No. C.159, maximum 1.0%

Production of High density polyethylene (HDPE)

HDPE containing TNPP is used in the manufacture of many products like blow-molded plastic drums or outer wrapping (film) of cigarette boxes or tea boxes.

Production of rubber

Rubber containing TNPP are used for example in tires and shoes soles.

Other applications

TNPP is used in other applications than plastic and rubber productions. Using the information provided in the SPIN database, it could be supposed that these other applications include the use of TNPP in publishing, printing and reproduction activities, in the manufacture of products of wood, of fabricated metal products, of furniture and in the construction activities. However, no more specific information is available.

Use of end-products

Shower curtains, flooring and wall coverings, bags and food packaging, blow-molded plastic drums, outer wrapping films, tires and shoes soles are examples of plastic and rubber end-products containing TNPP. For all these products, both private and professional end-uses may happen. As a worst case, private use will be considered for all uses in the EUSES program (E.C., 2004b). However, it could be expected that TNPP or NP releases due to the use of end-products are negligible.

Recovery and disposal

No information on recovery has been submitted. In view of the end-products containing TNPP that are manufactured, it could be assumed that products containing TNPP may be either recycled into new products, disposed in landfill or incinerated. Therefore, this stage could be considered in the EUSES calculation (E.C., 2004a). However, no default value is actually available for this stage in version 2.0 of the software.

TRENDS

Releases of TNPP and or NP (nonylphenol) to the environment occur during production, transport, storage, formulation and processing of plastic and rubber products. In addition, releases may also take place through the uses of the end-products. Finally, waste disposal of the end-products may also release TNPP or NP into the environment.

The different industry categories (IC), use categories (UC) and main categories (MC) used in the EUSES calculations are described in Table B.2.0.4

Table B.2.0.4: Industrial Categories (IC), Use Categories (UC) and Main categories (MC) used in EUSES calculations

Life cycle stages		IC	UC	MC	A-Table	B-Table
Production		11	49	I b	A 1.1	B 1.4
PVC films (2,800 t)	Formulation	11	49	III	A 2.1	B 2.3
	Processing	11	49	II	A 3.11	B 3.9

Life cycle stages		IC	UC	MC	A-Table	B-Table
LLDPE films (1,200 t)	Formulation	11	49	III	A 2.1	B 2.3
	Processing	11	49	II	A 3.11	B 3.9
HDPE films (800 t)	Formulation	11	49	III	A 2.1	B 2.3
	Processing	11	49	II	A 3.11	B 3.9
Rubber (2,960 t)	Formulation	11	49	III	A 2.1	B 2.3
	Processing	11	49	II	A 3.11	B 3.9
Others (200 t)	Formulation	15	55	III	A 2.1	B 2.3
	Processing	15	55	II	A 3.16	B 3.14

For tonnage input in the B tables, regional tonnage of TNPP was set to 700 t for the uses for PVC, LLDPE and rubber (maximum reported consumption range for TNPP processing facilities). For the uses in HDPE and other uses, the regional tonnage was respectively set to 800 t and 240 t.

A default fraction of TNPP in formulation is suggested in TGD (E.C., 2003) Emission Scenario Document for rubber Industry: up to 1.5 % (wt) for processing aids used as stabilisers. However, TNPP manufacturers have submitted better approximations of this value, for different formulated products (Personal communication from TNPP consortium, 1st April 2004):

- PVC film 0.8-1.5 %
- Polyolefins 0.1-0.2 %
- Rubber 0.4-1.0 %

As a worst case, the upper limit of these intervals will be used for the exposure assessment. Then, as a worst case too, fractions of the main source and number of days are derived from Tables B using the tonnage as such for each use.

B.2.3 Uses advised against by the registrants

None.

B.3 Classification and labelling

B.3.1 Classification in Annex I of Directive 67/548/EEC

TNPP chemical is not classified under Annex I of Directive 67/547 EEC.

Classification was finalised in the Commission working group on the Classification and Labelling of Dangerous Substances in November 2005 (human health):

Symbol : Xi
R-phrase : R43 : May cause sensitization by skin contact.

Classification for Environmental effects: to be updated.

B.3.2 Classification in classification and labelling inventory/Industry's self classification(s) and labelling

No data

B.4 Environmental fate properties

Parts of the assessment still have to be updated. Refer to chapter 3.1 of the RAR.

B.4.1 Degradation

B.4.2 Environmental distribution

B.4.3 Bioaccumulation

B.4.4 Secondary poisoning

B.5 Human health hazard assessment

B.5.1 Toxicokinetics

No specific toxicocinetic study was conducted with trisnonylphenyl phosphite (TNPP).

However qualitative information can be derived from the physico-chemical properties of the substance. Considering the relatively high molecular weight of the molecule (MW = 689 $g.mol^{-1}$), its extremely low water solubility and a very high Log P_{ow}, the absorption of TNPP by the gastro-intestinal tract is expected to be limited.

The vapor pressure of the liquid substance (physical state at 20°C and 101,3 kPa) is very low . Therefore, inhalative exposure can be anticipated only as liquid aerosol.

The molecular weight (> 500) of TNPP, its water solubility (< 1 mg/l) and its Log Pow (> 6) are in favour of a very limited absorption following dermal exposure.

Based on the physico-chemical properties , default values were chosen for oral, dermal and inhalative absorption :

Oral absorption: as indicated above, the absorption of TNPP by the gastro-intestinal tract is expected to be limited. However no quantitative value is available, then as a worst case assumption for oral route, a default value of 50% is chosen.

Dermal absorption: a default factor of 10% is used as MW>500 and Log P_{ow} is higher than 4.

Inhalative exposure: absorption mechanisms via mucous membranes are expected to be the same by oral and inhalation route, thus a default value of 50% is chosen as a worst case assumption.

B.5.2 Acute toxicity

This is a summary of the acute toxicity. For more details, refer to 4.1.2.2 of the RAR.

No human data is available. In animals, TNPP has a very low acute toxicity by the oral route, with a LD_{50} value of about 19.5 +/- 3.3 gram/kg bw for the rat. Hemorrhagic lesions in the gastro-intestinal tract and the lungs are seen in some animals, following the

administration of a lethal dose. This value was used for the risk assessment. The other studies couldn't be used in the risk assessment due to shortcomings or unavailable study reports. Furthermore a LD_{50} could not be derived from these studies as no mortality was observed at doses up to the highest doses tested (about 10 g/kg). Nevertheless, these results are in accordance with the value of 19.5 g/kg bw derived from the study from Naugatuck (1957).

The acute toxicity of TNPP by the dermal route seems to be very low too, with a LD_{50} greater than 2000 mg/kg in rabbits. No data is available on the acute inhalation toxicity, although the non-corrosive and non-irritant nature of TNPP (see section 4.1.2.3.1 on skin irritation) may suggest that toxicity would not be enhanced following exposure by this route.

By intraperitoneal route, the LD_{50} was found to be > 1000 mg/kg in rats.

Classification and labelling :

According to the criteria of the European Union, this chemical does not need to be classified on the basis of its acute toxicity.

B.5.3 Irritation

This is a summary of the irritation. For more details, refer to 4.1.2.3 of the RAR.

No information is available from human studies. Based on the available data on rabbits, it can be assumed that TNPP is a very slight to moderate irritant to the skin, varying according to tests conditions used : TNPP was a very slight irritant when administered to intact skin for a 4-hours exposure, whereas a 24-hour exposure on intact and abraded skin under occlusive conditions elicited more severe irritation properties. The two available studies indicate that TNPP is a slight irritant to the eye. In each case, the effects were generally reversed within a few days.

Classification and labelling :

According to the cutaneous and eye irritation test methods cited in Annex V, similar to OCDE guideline 404 and 405, TNPP should not be classified as an irritant to skin and eye.

B.5.4 Corrosivity

The results from the study of Tay (2001b) indicate that after a 4-hour exposure under semi-occlusive conditions TNPP is not corrosive on intact skin (OECD 404 conditions). However, the study conditions of another study (Ciba-Geigy, 1981) elicit corrosive properties of TNPP. These were harsh conditions (24h exposure under occlusive conditions on abraded and non-abraded skin), furthermore the study report indicates no further details on necrosis observed (was necrosis observed on intact or abraded skin? After what time of application the necrosis was observed?). Based on exposure conditions adopted by OECD guideline for classification, the results of the study of Tay were used in the risk assessment.

Classification and labelling :

TNPP should not be classified as corrosive to skin or eye according to the criteria of the European Union.

B.5.5 Sensitisation

This is a summary of the sensitisation. For more details, refer to 4.1.2.5 of the RAR.

No human data is available. The results of the Buehler sensitisation test and of the Maximisation test, both conducted on guinea pig and following OECD TG 406, are not in accordance.

Adjuvant-type tests are likely to be more accurate in predicting a probable skin sensitising effect of a substance in humans than those methods not employing Freunds Complete Adjuvant (FCA), and are thus the preferred methods. Then, the results of the Guinea-Pig Maximisation test will be used for the risk assessment, as this test is considered to be more sensitive than the Buehler test.

No information on respiratory tract sensitisation is available.

Classification and labelling :

TNPP needs to be classified as a skin sensitiser according to the criteria of the European Union (Xi, R43).

B.5.6 Repeated dose toxicity

This is a summary of the repeated dose toxicity. For more details, refer to 4.1.2.6 of the RAR.

For repeated dose toxicity, confidence is gained by the evaluation of several generations in the two-year studies. These studies provide a profile of limited repeated dose toxicity for TNPP.

A 90-day exposure to a dose of 5000 mg/kg/day (5%) of TNPP in rat resulted in the observation of toxic symptoms and of pathological changes in the kidney, but no adverse effect was observed at lower doses. Over a longer period (2-year), ingestion of TNPP at a dose level of 10 000 ppm (corresponding to 500 mg/kg/d in rats) led to a slight retardation of growth in male rats, an increase of the liver weight in F0 female rats and a thyroid change (doubtful relationship to dosage) in dogs. One male dog exposed to 10 000 ppm also exhibited a renal chronic inflammation in pelvis. In these 2-year studies, 3300 ppm of TNPP in the diet (corresponding to 167 mg/kg/d in rats), was derived as a NOAEL, both for rat and dog. In the modified and enhanced OECD TG 421 study with rats, the NOAEL for systemic toxicity was established at 200 mg/kg/day, based on an excessive rooting behaviour in males and females and on a treatment-dependent corticomedullary junction mineralisation of the kidney in males observed at the highest dose level (1000 mg/kg/day). However, microscopic examination was only performed on 5 males and 5 females of the control and the highest dose group, thus, the NOAEL could not be used for the risk assessment.

Based on this lack of information in the study of Tyl *et al.* and on the respective duration of the studies, the NOAEL used for risk assessment for repeated dose toxicity is 3300 ppm (corresponding in rats to 167 mg/kg), derived from the 2-year study in rat (Food and drug research laboratories) and based on the following limited effects: a slight retardation of

growth in males and an elevation of the absolute liver weight in F0 females. This NOAEL is rather conservative.

Factors such as hydration, diet, or intratubular pH may alter the mineral balance within kidneys (Montgomery *et al*, 1990 ; Kahn *et al*., 2002). Additionally, compounds with vitamin D activity could promote mineralisation. Compounds such as oestrogen or having estrogenic activity can influence mineralisation as well, however, the high-dose, F0 and F1 females did not show any evidence of increased severity of mineralisation. There are sex-related differences in the renal metabolism and handling of some xenobiotics in the rat kidney which could have also influenced this change. In particular female kidneys present some kind of down regulation to oestrogen-like compounds as they are exposed to a high level of oestrogens in physiological conditions, whereas male kidney which are not exposed to such a high level of oestrogen are more reactive to an oestrogen-like stimulation.

It could be suggested that abnormal rooting behaviour, reported in rats at 1000 mg/kg/day in the study of Tyl *et al*. (2002) could be linked with a neurotoxic activity of the test compound. However, "rooting in bedding" typically postdosing (but also predosing) in a dose-related incidence was observed in every gavage study performed in rats in the laboratory which conducted the study and in many others too. The consensus is that it is an expression of taste aversion, likely the animal's attempt to get rid of the bad taste in its mouth from the oral gavage dosing. The higher the dose, the more test material, the greater the incidence of rooting; in this study all rooting was observed postdosing. This behavior is therefore considered indicative of a conditioned adaptive behavior. Furthermore, abnormal behaviour was not observed in the other available studies. An unpublished study carried out by the Dutch National Institute of Public Health and Environment, on delayed neurotoxicity in chickens did not show any evidence of delayed neurotoxicity in chickens for TNPP (Van Velsen *et al*.,1980).

Classification and labelling :

This chemical is not classified according to the criteria of the European Union. R48 should not be applied.

B.5.7 Mutagenicity

This is a summary of mutagenicity. For more details, refer to 4.1.2.7 of the RAR.

In vitro mutagenetic tests did not reveal any genotoxic effect in six well-conducted tests, two Bacterial Reverse Mutation Assays, two *in vitro* Mammalian Cell Gene Mutation Tests, and two *in vitro* Mammalian Chromosome Aberration Tests.

Although neither human data nor *in vivo* tests are available, the available data from *in vitro* tests support the view that TNPP is a non-genotoxic substance.

B.5.8 Carcinogenicity

This is a summary of carcinogenicity. For more details, refer to 4.1.2.8 of the RAR.

There are no reliable study available on carcinogenicity, however, on the basis of the information currently available on mutagenicity, TNPP is considered as a non-genotoxic substance, so concerns for cancer caused by a genotoxic mechanism are low.

Considering the potential for carcinogenicity by a non-genotoxic mechanism, no evidence of a significant increase of tumour incidence was found in the 2-year chronic studies carried out on a small sample of rats and dogs.

Although only limited data are available, these data tend to indicate that TNPP is not of concern for a carcinogenic potential.

Classification and labelling :

This chemical is not classifiable as a carcinogen according to the criteria of the European Union.

B.5.9 Toxicity for reproduction

This is a summary of toxicity for reproduction. For more details, refer to 4.1.2.9 of the RAR.

TNPP exposure over four generations did not reveal any significant effect on reproduction up to 500 mg/kg/d, the highest dose tested, except for a possible reduction of litter size, born from F1 and F2 generations at the highest dose. This slight tendency seems to be confirmed by the OECD 421 study in which a slight but significant litter size reduction was observed at the highest dose (1000 mg/kg/day). In this same study, maternal toxicity was observed at the dose of 1000 mg/kg/day. At the dose of 1000 mg/kg/day, a decrease of the ovary weight of F0 females and the decrease of epididymides weight in F1 males suggest an oestrogen-like activity of the test substance. No other significant effects on reproductive toxicity were observed in this study.

Phenomenon of dystocia observed in dams at the highest dose in the study of Tyl (2002) is viewed as maternal toxicity, due from the adjustments of dosing volume on gd 14 and especially on gd 20, resulting in over dosing the dams in late gestation. Actually, the dosing volume of the test chemical was adjusted for each dam based on each new body weight. This means that the dosing volumes for the F0 dams during gestation were adjusted on gd 0, 7, 14, and 20. The pregnant rat CD (SD) females gain approximately 150 g or more during gestation but with the body weight gain from gd 14 to parturition (the “last trimester”) of at least 100 g, due almost entirely to the rapid growth of the uterine contents. For gavage studies, test chemical intake (in mg/day) during this period is increased by as much as 30% because of the adjustment for maternal body weight, especially from gd 20 to parturition (gd 22 ± 1). Thus, the dose in mg/kg/day, based on the actual maternal body weight minus the uterine contents, is similarly increased by ~30%. This can result in overdosing the dam (and conceptuses) and is likely the cause of the excessive peri-parturitional maternal toxicity observed.
The risk of increased maternal toxicity in late pregnancy from bolus gavage dosing is due to: (a) the maternal liver (although it is enlarged in late pregnancy in response to the pregnancy and the increased test chemical load) is not enlarged commensurate with the increased test chemical dose; (b) test chemical is likely not equally distributed between maternal and fetal compartments, so the relative maternal burden may be even greater; and

(c) gastrointestinal tract motility is reduced in late pregnancy, so there is likely increased absorption of the test chemical from the gut due to longer transit times.

Based on these observations, the NOAELs for reproductive toxicity and for maternal toxicity were 200 mg/kg/day, derived from the OECD 421 study (considered as a key study for risk characterisation as a recent study, following OECD guideline).

No indication of any developmental effect was observed in both of the studies. $NOAEL_{terato}$ is ≥ 1000 mg/kg/day, although these parameters were observed on a very reduced number of animals.

Classification and labelling :

This chemical is not classified as toxic to reproduction (fertility and development) according to the criteria of the European Union.

B.5.10 Other effects

none

B.5.11 Derivation of DNEL(s)/DMEL(s) or other quantitative or qualitative measure for dose response

Not calculated

B.6 Human health hazard assessment of physico-chemical properties

B.6.1 Explosivity

TNPP has no explosive properties.

B.6.2 Flammability

TNPP has a very low degree of flammability (flash point : 207°C).

B.6.3 Oxidising properties

TNPP has no oxidising potential.

B.7 Environmental hazard assessment

To be updated. Refer to chapter 3.2 of the RAR.

B.7.1 Aquatic compartment (including sediment)

Refer to chapter 3.2 of the RAR.

B.7.2 Terrestrial compartment

Refer to chapter 3.2 of the RAR.

B.7.3 Atmospheric compartment

Refer to chapter 3.2 of the RAR.

B.7.4 Microbiological activity in sewage treatment systems

Refer to chapter 3.2 of the RAR.

B.7.5 Non compartment specific effects relevant for the food chain (secondary poisoning)

Refer to chapter 3.2 of the RAR.

B.8 PBT and vPvB assessment

This part corresponds to the chapter 3.3.6 of the RAR in annex.

B.8.1 PBT assessment for TNPP

- The P/vP screening criterion is fulfilled as the substance is non readily biodegradable based on a negative result at a test on ready biodegradability performed according to OECD guidelines 301B and 301D. It has been shown than the substance can be hydrolysed into nonylphenol, this hydrolytic product being readily biodegradable. However, hydrolysis was not considered to be significant in environmental conditions. The low mineralization observed in ready biodegradation test would allow considering the substance as P/vP although further testing would be necessary for a definite assignment.
- The screening B/vB criterion is fulfilled based on the bioaccumulation potential determined with log Kow worst case values for QSAR models. A log BCF of 2.68 has been calculated for fish (TNPP log Kow >10) and a log BCF of 6.07 has been calculated for earthworm (TNPP log Kow maximum value of 8). However, while considering the measured log Kow of 14 and additional information on the molecular weight and the size of the molecule, there might be indications that the above calculations overestimate the bioaccumulation potential of the substance (section **Erreur ! Source du renvoi introuvable.**). Further testing would be necessary for a definite assignment.
- Concerning the T criterion, no aquatic toxicity is expected at concentrations above the water solubility of TNPP based on the available set of information. However, a long-term test with daphnids is requested.

Conclusions to PBT assessment

(i) There is a need for further information and/or testing.

- Based on the available data, TNPP would be classified as vPvB. However, only the screening criteria are fulfilled for the P/vP criterion. Likewise, the vB criterion is fulfilled based on a BCF calculated from an estimated log Kow taken as a worst case. The T criterion remains inconclusive, pending the results of a new long-term toxicity test on daphnids. Refinement of these 3 parameters is necessary to conclude the PBT assessment of this chemical.

B.8.2 PBT assessment for NP

Properties of NP have been extracted from the EU risk assessment report available for this substance (E.C., 2002).

- Nonylphenol is considered inherently biodegradable. However, a half-life in surface water has been estimated at 150 days. Hence the vP criterion is fulfilled (half-life > 60 days).
- The B criterion is not fulfilled based on the BCF of 1,280 used in the European risk assessment report (BCF < 2000).
- The T criterion is fulfilled since NOECs < 0.01 mg/L have been identified for fish and invertebrates for example.

Based on the properties of nonylphenol, it appears that nonylphenol is neither PBT nor vPvB.

B.9 Exposure assessment

B.9.1 General discussion on releases and exposure

B.9.2 Occupationnal exposure

This part includes only a summary of the occupational exposure which can be found in more details in chapter 4.1.1 of the RAR in annex.

Table 9-2: Summary of reasonable worst case exposures

Scenario	8-hour TWA inhalation (mg/m³)	Dermal (mg/day)
1 - Manufacture	2.86	0-42
2 – Manufacture of products	8.58	42 - 420
3 – Use of preparations	5.72	0.42 - 4.2

B.9.3 Consumers exposure

Consumer exposure can occur from migration of TNPP from food contact materials The overall potential dietary exposure, or total estimated daily intake (TEDI), to TNPP from the use in food-contact packaging is 0.0337 mg/day. For more details about the assessment of the consumer exposure, refer to chapter 4.1.1.3 of the RAR.

B.9.4 Human exposed via the environment

Not provided as environmental risk assessment has to be updated before.

B.9.5 [Summary of] environmental exposure assessment

Refer to chapter 3.1 of the RAR in annex.

B.9.6 Combined human exposure assessment

B.10 Risk characterisation

B.10.1 Human health

B.10.1.1 Workers

For more details, refer to chapter 4.1.3.2 of the RAR.

Table 1: Overview of the conclusions with respect to occupational risk characterisation

	Conclusions valid for the occupational scenarios					
	Scenario 1		Scenario 2		Scenario 3	
	MOS	Conl.	MOS	Concl.	MOS	Concl.
Acute toxicity						
- $LD50_{dermal}$ > 2000 mg/kg	n.a.	ii	n.a.	ii	n.a.	ii
- $LD50_{oral}$ > 10000 mg/kg	n.a.	ii	n.a.	ii	n.a.	ii
Irritation						
- skin	n.a.	ii	n.a.	ii	n.a.	ii
- eye	n.a.	ii	n.a.	ii	n.a.	ii
Sensitisation						
- dermal	n.a.	**iii**	n.a.	**iii**	n.a.	**iii**
Repeated Dose Toxicity, systemic effects						
- oral (rat, 167 mg/kg/day)	321	ii	69	ii	199	ii
Mutagenicity	n.a.	ii	n.a.	ii	n.a.	ii
Carcinogenicity	n.a.	ii	n.a.	ii	n.a.	ii
Reproductive toxicity, fertility						
-oral (rat, 200 mg/kg/day)	385	ii	87	ii	238	ii
Reproductive toxicity, developmental effects	n.a.	ii	n.a.	ii	n.a.	ii

n.a. not applicable

Conclusion iii is derived for sensitization in all scenarios (manufacture of the substance, manufacture of products and use of preparation). According to the risk evaluation, the conclusion is mitigated given the non dispersive use of the substance and the lack of reported case of sensitisation.

B.10.1.2 Consumers

Repeated dose toxicity and reproductive effects are of low concern (**conclusion ii**). For more details, refer to chapter 4.1.3.3 of the RAR.

B.10.1.3 Indirect exposure to humans via environment

Not provided as the environmental risk assessment has to be updated before.

B.10.2 Environment

Conclusions of the environmental part of the risk characterisation have been extracted from the RAR. For more details on the risk characterisation, refer to chapter 3.3 of the RAR in annex.

Conclusions to the risk assessment for the aquatic compartment

Sewage treatment plants (exposure to TNPP and NP)

(ii) There is at present no need for further information and/or testing or for risk reduction measures beyond those that are being applied already.

This conclusion applies to all stages of the life cycle of TNPP.

Freshwater (exposure to TNPP)

(i) There is a need for further information and/or testing.

This conclusion applies to all stages of the life cycle of TNPP.

- There is a need for more information for the effect assessment of TNPP. A long-term testing on Daphnia is requested.

Update on the work performed to answer this request: a short-term test with daphnids has been performed by Industry. However, some drawbacks associated with the chemical analysis were identified during the test and the study should be considered invalid (low recovery rates found with the TNPP analysis; too high nominal concentrations of TNPP tested leading to sufficient residual NP concentrations to generate an effect). Based on this experience, a new test is currently being setting-up.

Sediment (exposure to TNPP)

(iii) There is a need for limiting the risks; risk reduction measures that are already being applied should be taken into account.

This conclusion applies to all stages of the life cycle of standard TNPP.

OR

(i) There is a need for further information and/or testing.

This conclusion applies to all stages of the life cycle of standard TNPP.

- Concerning the sediment compartment, one long term study is available on the toxicity of TNPP toward endobenthic organisms and associated with an Assessment Factor of 100 to calculate the PNEC. Considering the low solubility in water and the high adsorption potential of TNPP, toxicity on sediment dwelling organisms should be further studied. Toxicity testings on sediment organisms should be done for the refinement of the PNECsed.

- A refinement of the information used to calculate the PEC or site monitoring should be considered afterward if a RCR >1 is calculated and a risk is still identified.

Conclusions to the risk assessment for the marine compartment
This section will be added when the exposure part for the aquatic compartment (freshwater and freshwater sediment) will be refined.

Conclusions to the risk assessment for the terrestrial compartment

Soil (exposure to TNPP)

(i) There is a need for further information and/or testing.

This conclusion applies to all stages of the life cycle of TNPP.

- Considering the suspected high adsorption potential of TNPP, toxicity on soil organisms should be studied. Based on the outcome of the long-term Daphnia study a PNECsoil sould be calculated with the equilibrium partitioning method. Toxicity testing on soil organisms should be performed subsequently for the determination of the PNECsoil in case a risk is identified for this compartment.

Conclusions to the risk assessment for the air compartment

No risk characterisation can be carried out for the air compartment since there is no specific effect data.

Conclusions to the risk assessment for secondary poisoning

Secondary poisoning (exposure to TNPP)

(ii) There is at present no need for further information and/or testing or for risk reduction measures beyond those that are being applied already.

This conclusion applies to all stages of the life cycle of TNPP.

- There are already indications that the bioconcentration factor of TNPP could be low (Cf. Annex 2 and section 3.1.1.2.5).

B.11 Summary of existing legal requirements (current risk reduction measures)

B.11.1 For workers

This part is extracted from the Risk Reduction Strategy which has been discussed and agreed at the last RRSM in april 2008 (see Handover-no ch-ES-11b-2008 Draft HH Recommandation Annex TNPP.doc in annex).

Classification and labelling

TNPP is not classified under Annex I of directive 67/548/EEC. Classification for human health effects was finalised in the Commission working group on the Classification and Labelling of Dangerous Substances in November 2005. Classification for environmental is not finalised and is subject to the conclusions of the TCNES.

Human health effects (adopted classification)

Symbol : Xi
R-phrase : R43 : May cause sensitisation by skin contact.
S-Phrases: S2: Keep out of the reach of children
S24: Avoid contact with skin.
S37: Wear suitable gloves.
S46: If swallowed, seek medical advice immediately and show this container or label

Environmental effects

To be updated

According to the preparations directive 1999/45/EEC even preparations that have not to be classified as sensitising but contain more than 1 % of a sensitising substance must have a special information on the package: “Contain “name of sensitising substance”, May cause allergic reactions.

As a result of its classification as hazardous substance, TNPP is subject to general regulations concerning its supply and handling.

Safety data sheets

In accordance with article 31 (title IV) of Regulation (EC) No 1907/2006, the supplier of a substance or a preparation that meets the criteria for classification as dangerous in accordance with Directives 67/548/EEC or 1999/45/EC shall provide the recipient of the substance or preparation with a safety data sheet compiled in accordance with Annex II.

The information system for hazardous substances and preparations in the form of labelling and the safety data sheets is considered sufficient in principle to provide the user with

sufficient information for the selection of suitable occupational safety measures. The SDS should contain all relevant information from the risk assessment report.

Occupational safety and health regulations

At the European level, the following directives are primarily applicable as general regulations for occupational safety and health of workers in the production and use of TNPP:

- 98/24/EC on the protection of workers from the risk related to exposure to chemical agent at work.
- 89/656/EEC on the use of personal protective equipment

Only limited knowledge is available about the extent to which the EU member states have in each case transposed these basic requirements into national law.

Occupational exposure Limits

There are no occupational exposure limits for TNPP. Considering the effect of concern and the low vapour pressure of TNPP, the fixation of an occupational exposure limit is not relevant.

Personal Protection Equipment (PPE) against dermal exposure

According to community Legislation, workers have to be provided with suitable PPE if their health is at risk due to exposure against chemicals. PPE that protects against the risks of TNPP is available and has to be indicated in the SDS. On account of the sensitising effect of TNPP the use of suitable protective equipment is general widely accepted and legally required, if dermal exposure cannot be excluded by other technical or organisational measures.

Conclusion of the RRS (workers)

Because this risk of sensitisation can neither be quantified nor excluded (based, for example, on the assumption that proper personal protection use and work procedure might not be applied in most of the plants handling TNPP in EU), a general concern for skin sensitisation is expressed in all workers scenarios. This conclusion was mitigated given the non dispersive use of the substance and the lack of reported case of sensitisation at the existing production sites. Furthermore, as it is reported in the risk assessment report, risk reduction measures which should be applied as a result of the classification of TNPP as the proper use of personal protective equipment can effectively reduce sensitisation at the work place.

The legislation for workers' protection currently in force at Community level is generally considered to give an adequate framework to limit the risks of the substance to the extent needed and shall apply. There are no further risks reduction measures proposed but, in order to ensure an effective enforcement of the current occupational regulation, there is a need to make the classification legally binding (i.e. TNPP should be added to the annex I of the directive 67/548/EEC or annex VI of the GHS regulation). As soon as the conclusions of the TCNES for the environmental classification are finalised, TNPP should be added to the next ATP proposal.

B.12.2 For consumers

Not relevant (conclusion ii).

C. AVAILABLE INFORMATION ON ALTERNATIVES

Not relevant at this stage of the dossier.

G. STAKEHOLDER CONSULTATION

Consultation took place during the risk assessment which is still ongoing (conclusion (i) for the environmental part).

REFERENCE

ANNEXES


R427_0307_hh.doc


R427_0810_env.doc


ES-11-2008 Draft RRS HH TNPP.doc


Handover-no ch-ES-11b-2008 Draf