P-TERT-BUTYLPHENOL

CAS No: 98-54-4

EINECS No: 202-679-0

SUMMARY RISK ASSESSMENT REPORT

Final report 2008

FINAL APPROVED VERSION

Norway

Rapporteur for the risk assessment of p-tert-butylphenol is the Norwegian Pollution Control Authority in consultation with the Directorate of Labour Inspection, on behalf of the European Union. The scientific work on this report has been prepared by the National Institute of Public Health, the Norwegian Institute of Water Research and the National Institute of Occupational Health.

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Final report:	**2008**

The last full literature survey was carried out in 2002 for HH and in 2004 for ENV. Targeted searches have been carried out subsequently for example on micronucleus test, endocrine effects. Toxicity data have been added until 2006 and exposure data until 2007 for consumers.

PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance para-tert-butylphenol that has been prepared by Norway in the context of Council Regulation (EEC) No. 793/93 on the evaluation and control of existing substances.

For detailed information on the risk assessment principles and procedures followed, the underlying data and the literature references the reader is referred to the comprehensive Final Risk Assessment Report (Final RAR) that can be obtained from the European Chemicals Bureau [1]. The Final RAR should be used for citation purposes rather than this present Summary Report.

[1] 1 European Chemicals Bureau – Existing Chemicals – http://ecb.jrc.it

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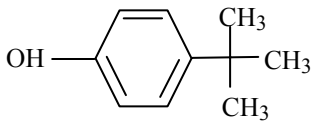
Tables:

1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS Number: 98-54-4
EINECS Number: 202-679-0
IUPAC Name: 4-(1,1-Dimethylethyl)phenol
Molecular formula: C10H14O

Structural formula:



Molecular weight: 150.22 g/mol

Synonyms: 4-tert-Butylphenol, p-tert-Butylphenol
Phenol, 4-(1,1-dimethylethyl), Butylphen

1.2 PURITY/IMPURITIES, ADDITIVES

Purity: ≥96 % (w/w) (SASOL, Germany GmbH).

Formation of 2,4,6-tri-tert-butylphenol during the production of p-tert-butylphenol theoretically is possible and can not be fully excluded. However, the material is not detected in the final product. The detection limit for 2,4,6-tri-tert-butylphenol in the final product (p-tert-butylphenol) is below 2 ppm. The situation for 2,4-di-tert-butylphenol is similar.

1.3 PHYSICO-CHEMICAL PROPERTIES

A summary of physico-chemical information on p-tert-butylphenol (ptBP) which is used in further calculations is shown in Table 1-1.

Table 1-1: Summary of physico-chemical properties of ptBP

Property	Value
Physical state	White flakes at 20° C
Melting point	Ca 100°C
Boiling point	237.5° C at 1,013 hPa,
Relative density	0.92 g/cm3 at 110 ° C

Vapour pressure	0.5 Pa at 20° C,
Water solubility	610 mg/l at 20° C (mean value)
Partition coefficient n-octanol/water (log value)	3.29 (OECD 107)
pKa	10.16 ,at 25°C, (OECD 112)
Granulometry	-
Conversion factors	-
Flash point	About 115° C
Autoflammability	510° C, (DIN51794)
Flammability	-
Explosive properties	-
Oxidizing properties	-
Viscosity	2.4 mPa s, at 110° C
Henry´s Law constant (calculated)	0.123 $Pa*m^3*mol^{-1}$ at 20° C,

1.4 CLASSIFICATION

P-tert-butylphenol is not classified according to Annex I of Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances.
Producers currently classify the substance as:

Human Health: Xi, R36/37/38

Environment: N, R51/53

1.4.1 Proposed classification

The Technical Committee on Classification and Labelling (TC C&L)in EU have agreed to classify ptBP as follows but it was not included in Annex I of Directive 67/548/EEC since the classification was agreed in the TC C&L group after the closure of the 31. ATP to the 67/548/EEC directive. It will be included in an ATP to the CLP regulation.

Repr. Cat. 3; R62[2]
Xi; R37/38-41 [3],
N; R51-53 [4],

1. [2] Commission Working Group on the Classification and Labelling of Dangerous Substances Meeting on Health Effects of Existing Chemicals, Pesticides & New Chemicals September 26-28, 2007
2. [3] Commission Working Group on the Classification and Labelling of Dangerous Substances Meeting on Health Effects of Existing Chemicals, Pesticides & New Chemicals March 21-24, 2006
3. [4] Commission Working Group on the Classification and Labelling of Dangerous Substances Meeting on

Symbol: Xn harmful
N dangerous for the environment

Risk phrases:

R 51-53: Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
R 37/38: Irritating to respiratory system and skin
R 41: Risk of serious damage to eyes
R 62: Possible risk of impaired fertility

Safety phrases:

S 2: Keep out of the reach of children.
S 26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
S 36/37/39: Wear suitable protective clothing, gloves and eye/face protection.
S 46: If swallowed, seek medical advice immediately and show this container or label.
S 61: Avoid release to the environment. Refer to special instructions/Safety data sheets.

2 GENERAL INFORMATION ON EXPOSURE

2.1 PRODUCTION

P-tert- butyphenol was produced by three companies in Germany, France and Switzerland[5] in 2001. From 2004 there were only two producers left. One producer was almost exclusively using ptBP for its own need (about 95%) on site. In 2001 the total tonnage ptBP used in EU was 26,617 t/a. This is based on a production volume of 25,251 t/a, including 2,100 t/a import and 734 t/a export of ptBP. No updated figures for 2004 have been provided and therefore data from 2001 were used.
PtBP is produced in a controlled closed system. Production of derivatives is also performed in controlled closed systems, although the processes itself may differ.
Phenol and isobutene are reacted in the presence of a fixed bed ion exchange resin in either a continuous process (2 producers) or a batch process (one producer). Following reaction the product is distillated to eliminate unreacted starting materials (these are directed back to the reactor). In a distillation step the final product is separated. The pure product is stored as a molten product at 130 °C under a nitrogen blanket and shipped in trucks. Due to the storage conditions releases to the atmosphere during storage are completely excluded. Another part of the molten product is processed to flakes in a strictly closed system. The flakes are automatically filled into 25 kg bags or "big bags" (about 400-800 kg).

2.2 USES

The major use is as a monomer in chemical synthesis, e.g. for the production of polycarbonate, phenolic resins, epoxy resins.

PtBP is used as a chain terminator in the synthesis of polycarbonate polymers. The main uses of polycarbonate are in compact discs, DVD and CD Rom manufacture. Furthermore polycarbonate is used in solid and multi-wall sheet in glazing applications and films and as polycarbonate blends for diverse injection moulded functional parts. Polycarbonate is also used in containers for storage of food and beverages and tableware.

The application of phenolic resins are as intermediates in contact and pressure sensitive adhesives, coatings, printing inks and electrical varnishes. A further use is for tack improvement in rubber compounding (tyre manufacture) and phenolic resins are ethoxylated for the production of oilfield chemicals (specialised surfactants).

Epoxy resins are used as hardening agents in paints and varnishes and in industrial corrosion protective coatings. Epoxy resins are used in linings for cans used for canned foods.

Furthermore ptBP is also used in the manufacturing of the corresponding cyclic alcohol (p-tert-butylcyclohexanol) and based on recent information from industry during the risk reduction process ptBP is also used in the production of tri-aryl phosphate esters, which are used as flame retardants and plasticizers.

[5] Although Switzerland is not a member of the EU, the production site in Switzerland is included for the risk assessment (production volumes are treated as EU production, "import" figures only relate to import from overseas).

Regarding consumers the main exposure from final products is expected to be from adhesives and possibly canned food. Consumers may also be exposed to ptBP in drinking water from drinking water reservoirs coated with epoxy-based paints or from pipelines. Consumers may moreover be exposed to ptBP from polycarbonate used for food contact material.

2.3 LEGISLATIVE CONTROLS

The Directive on Plastic Materials and Articles Intended to Come into Contact with Foodstuffs (2002/72/EEC)

PtBP is on the "positive" list in Annex II "List of monomers and other starting substances which may be used in the manufacture of plastic materials and articles", Section A, with a legally binding specific migration limit (SML) of 0.05 mg/kg (50 ppb).

Chemical Agents Directive (98/24/EEC)

No occupational exposure limit value (OEL) have been established for ptBP at Community level, but a few Member States have established national limits values of (0.5 mg/m^3) 8 hour time weighted average.

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

3.1.1 Environmental releases

Life cycle steps with potential release to the environment are the production of ptBP itself, processing, as well as potential releases of residual ptBP from the processed goods (e.g. resins, polycarbonate) or finished products and from disposal of ptBP containing products.

The number of ptBP production sites is limited and monitoring data are partly available. A generic release calculation using the TGD/EUSES model has been performed for information and comparison with the site specific scenarios. For the local release calculations actual figures (e. g. release figures, WWTP data) have been used for the production sites.

For the processing step phenol/formaldehyde resins production several users of the material have provided information regarding use and exposure in 2001 and a water monitoring program was carried out in 2005/06. This information has been used to estimate the local releases of ptBP and to calculate local concentrations. For all sites providing sufficient monitoring data no risk was identified. However, to cover the releases from those sites where no or inadequate information is available (which was ca 53 % of the market) a generic scenario has been applied. For the phenol/formaldehyde resin production generic scenario, however, the release factor to waste water was raised compared to the TGD release. The exposure assessment is based on the average emission factor obtained from the site participating in the EPRA water monitoring program that had the highest emission to waste water. This site had however a highly efficient waste water treatment system in place and no risk to surface water was identified for this site. Apart from the emission factor to waste water the default parameters from the TGD were used. According to recent information from industry during the risk reduction phase one of the sites (site 5) , originally reported amongst the phenol/formaldehyde resin production sites, uses ptBP in the production of tri-aryl phosphate esters. The emission scenario had been considered to be comparable to the phenolic resins production scenarios. The risk assessment concluded, however, that more information is needed for this site. For phenolic resin production site 6 no site specific data is available. Further exposure information is needed in order to calculate a $PEC_{aquatic}$ and a PEC_{STP} for this site.

Concerning the production of epoxy resins no site specific data on emissions has been obtained by industry but only qualitative descriptions of the processes involved. The information received resulted in four sub-scenarios, which have been proposed by industry. TGD default parameters have been used to calculate environmental concentrations. The TGD release factor to waste water has been lowered due to information from industry for sub-scenario 4.

Releases of ptBP during the use of the finished products are generally low or negligible. For example polycarbonate have a residual level of free ptBP of <5 ppm. However, as described in the RAR cured epoxy systems may still contain significant amounts of unreacted ptBP (up to 5-10 %). In general, high temperature cured epoxy formulations are not expected to release

significant quantities because of low residual amounts of free ptBP. This applies especially for can coatings. Regarding use of epoxy resins for food contact, the emission limits (SML) for food contact material have to be fulfilled. However, it is state-of-the-art knowledge that ambient cured epoxies have significantly lower level of thrue-cure than epoxies cured at high temperatures. No data on release from ambient cured epoxy products have been provided.

A summary of estimated PECs for the different compartment is shown in Table 3-1. When site specific information is used to establish the PECs the highest PEC estimated for each use category is used. When no site specific information is available, estimated PEC values are calculated with EUSES according to the TGD. Local PECs ranged from < 0.02 µg/l to 775 µg/l for the aquatic/marine compartment and from 20 µg/kg wwt to 4830 µg/kg wwt for agricultural soil. Regional PECs were estimated by EUSES to 0.009 µg/l for marine water, 0.095 µg/l for surface water and 0.04 µg/kg wwt for agricultural soil.

Table 3-1: Estimated local PEC for the different compartments

Use category	PECaquatic [µg/L]	PEC marine [µg/L]	PEC STP [mg/L]	PECsoil [µg/kg] wwt
Production- Site specific, site B	0.11		0.02	
Phenolic resins (water monitoring program)			0.01	
Phenolic resins				
Site specific, site 4	0.66			
Site specific, site 5, marine [1]		tonnage confidential	tonnage confidential	
Site specific, site 8 marine		< 0.02	0.01	
Phenolic resins TGD, generic scenario	178		1.78	1,110
Polycarbonate resins Site specific, location A	0.10		0.0013	
Epoxy resins				
TGD, generic scenario	775		7.75	4,830
Sub-scenario 1	1.94		0.02	20
Sub-scenario 2+3	194		1.94	1210
Sub-scenario 4				

Regional PEC	0.095	0.009		0.04

1) For site 5 ptBP is used in the production of tri-aryl phosphate esters. The emission scenario is considered to be comparable to the phenolic resins production scenarios.

3.1.2 Environmental fate

Due to its water solubility releases of ptBP are expected primarily to the aquatic compartment. To a limited extend release to air and to soil can be expected. General characteristics of ptBP which are relevant for the exposure assessment are given below.

Degradation

PtBP will be rapidly removed from the air compartment through a combination of photodegradation and OH-radical degradation giving a half life of 0.4 days. In addition the water solubility of 610 mg/l will result in rapid deposition of any ptBP present in the atmosphere during rain.

Concerning biodegradability there are conflicting results available. According to test results from a DOC-Die-Away test ptBP can be regarded as readily biodegradable meeting the 10 day window criterion. However, the inoculum in the DOC-Die-Away test might have been adapted to ptBP as it was taken from a predominantly municipal STP from a heavily industrialised area. The results from a Manometric Respirometry Test show that ptBP is ready biodegradable but failing the 10 day window. The monitoring values from different STPs in Austria, which are above the detection limit, support the conservative approach characterising ptBP as readily biodegradable not fulfilling the 10 day window criterion. Therefore as a worst case, ptBP is considered as readily biodegradable without meeting the 10 day window. No information on degradation in soil has been submitted. The half life of 50 days in surface water and a half life of 90 days in soil is therefore assumed for the risk assessment.

Distribution

The Henry's law constant of 0.123 Pa m^3*mol^{-1} indicates that ptBP is not likely to volatilize from surface waters. Rapid degradation in the atmosphere and relatively high water solubility indicates that ptBP, which is released to the atmosphere and not degraded there, will precipitate during rainfall. A Koc-value of 582 is estimated based on a log Kow of 3.29. Experimental data and calculated partition coefficients indicate that ptBP will have a low mobility in soil.

Bioaccumulation

The Log Kow of ptBP is 3.29, resulting in a calculated BCFfish of 125 indicating a potential for bioconcentration. A BCF of 120 in *Leucicus idus melanotus* was measured and this value has been used in the exposure calculations.

For the assessment of the bioaccumulation potential of a substance not only the lipophilicity but also the biotransformation and subsequent elimination from the organism has to be taken into account as well. Phenolic materials are rapidly glucuronidated and/or sulphated followed

by excretion via the urine or faeces. The principal metabolic pathways are not only available in mammalian organisms, but also in aquatic organisms (e. g. fish). It is therefore concluded that available data indicate that ptBP is unlikely to bioaccumulate in the food chain.

3.2 EFFECTS ASSESSMENT

3.2.1 Aquatic compartment

Acute test data are available for fish, invertebrates and algae, covering three different trophic levels.. The lowest available NOEC is 320 µg/l from a 72 h algae toxicity test with *Selenastrum capricornutum.* According to the TGD the algae test can be regarded as a chronic test, since, under technical aspects, it covers several generations. Therefore two chronic tests are already available. Since the NOEC includes invertebrates which was the trophic level showing the lowest L(E)C50, the TGD allow reducing the application factor to 50.

$PNEC_{aquatic}$ =320 µg/l /50 = 6.4 µg/l

For deriving a $PNEC_{marine}$ an assessment factor of 500 has to be applied to the NOEC for algae because only two long-term NOECs from freshwater or saltwater species representing two trophic levels (algae and crustaceans) are available.

$PNEC_{marine}$=320 µg/l /500 = 0.64 µg/l

However the PNECaquatic is provisional.

PtBP belongs to a group of chemicals known as alkylphenols. Alkylphenols have been suspected to cause endocrine disruption in wildlife. In vitro data on ptBP are available and read across from similar alkyl phenol compounds, including p-tert-pentylphenol, have shown estrogenic effects in vivo. For ptBP also a pilot extended early life stage fish study with fathead minnow (*Pimephales promelas*) has been performed at nominal concentrations of 1, 30,100 and 500 µg/l . The main results of the pilot study was that the most sensitive endpoints were delayed hatching, presence of intravascular fluid in female gonads and the presence of fatpads and fatpad score in male fish. The study thus suggests a NOEC of 25 ug/l (30 ug/l) and a LOEC of 82 ug/l (100 ug/l). The provisional NOEC could be supported by reading across to data on p-tert-pentylphenol, however there were concerns about a potential reduction of vitellogenin (Vtg) levels in females at low concentrations as indicated by the data from the pilot study. There is concern that even if read-across to the available data on p-tert-pentylphenol may be appropriate for certain EDC mediated mechanisms such as feminization of males, there is a large uncertainty related to whether potential effects on female reproductive parameters will be covered by read-across to p-tert-pentylphenol based on the data presently available. The level of uncertainty in the present available data was proposed to bee too high to abandon the definitive extended early life stage fish study. The fish study will be performed and the results will be published in an addendum to the risk assessment report.

No test is available for sediment dwelling organisms. According to the TGD the equilibrium partitioning method may be used to estimate the $PNEC_{sediment}$. However, as no direct

measurements of ptBP are available from sediment, PEC concentrations would have to be estimated in the same fashion giving the same PEC/PNEC ratios as for surface water. Therefore a $PNEC_{sediment}$ has not been derived.

3.2.2 Sewage treatment plant

A test with *Pseudomonas putida* gave an EC10 of 140 mg/l and is therefore less sensitive than the toxicity control in the ready biodegradability test "Manometric Respirometry Test (OECD 301 F). In this ready biodegradation test results with the toxicity control indicated that biodegradation of aniline was inhibited at 25 mg/l of ptBP. At a concentration of 15 mg/l degradation proceeded satisfactory but with a lag phase. This value should be applied as an EC10 with an assessment factor of 10 giving a

$PNEC_{micro\text{-}organisms}$ of 1.5 mg/l.

3.2.3 Terrestrial compartment

There are no toxicity tests available with respect to the terrestrial compartment. The derivation of the PNEC for the terrestrial compartment must therefore be performed applying the partition equilibrium method of the TGD. ($PNEC_{soil}=K_{soil\text{-}water}/RHO_{soil}*PNEC_{aquatic}*1000$)

PNECsoil=19.5 / 1700 * 6.4 * 1000 = 73 µg/kg wwt

3.2.4 Atmosphere

No information is available or needed at this stage due to low exposure of the atmosphere and the short half life of ptBP when released to the atmosphere.

3.2.5 Secondary poisoning

Available data indicate that ptBP is unlikely to bioaccumulate in the food chain. No further information is considered necessary with respect to effects through the food chain.

3.2.6 PBT assessment

In the PBT assessment the following criteria are used to decide if a substance must be regarded as a PBT substance.

- P (Persistence): Half-life > 60 d in marine water or > 40 d in freshwater or half-life > 180 d in marine sediment or > 120 d in freshwater sediment.
- B (Bioaccumulation): BCF > 2,000.
- T (Toxicity): Chronic NOEC < 0.01 mg/l or CMR or endocrine disrupting effects.

PtBP is readily biodegradable, but not meeting the 10 day window criterion. It is not fulfilling the persistency criterion. The measured BCF of 120 is far below the B criterion. The T criterion is fulfilled since ptBP is agreed classified as toxic for reproduction (category 3). However, for a selection as a PBT substance all three criteria have to be met.

3.3 RISK CHARACTERISATION

3.3.1 General discussion

This assessment concludes that the aquatic compartment is the one of main concern with respect to the use of ptBP. The risk characterisation is therefore performed for this compartment. No site specific information on either concentration in sediments or on effects on sediment dwelling organisms is available. In the absence of both these entities, PEC and PNEC would have to be estimated according to the partitioning method giving the same PEC/PNEC ratio as for surface water.

3.3.2 Aquatic compartment (incl. sediment)

In Table 3-2 risk characterisation is performed using a PNECaquatic of 6.4 µg/l. This is only a provisional assessment as there is a request to perform a chronic fish test that may change the aquatic PNEC.

Table 3-2: Estimated local PEC/PNECs for the aquatic compartment (including sediment)

Use category	Estimation method	PECaquatic [µg/l]	PEC/PNEC
Production	Site specific, site B	0.11	0.02
Phenolic resins*	Site specific, site 4	0.66	0.10
Phenolic resins	TGD	178	**28**
Polycarbonate resins	Site specific, location A	0.10	0.02
Epoxy resins	TGD		
Sub-scenario 1		775	**121**
Sub-scenario 2+3		1.94	0.30
Sub-scenario 4		194	**30**
Regional PEC surface water	TGD	0.095	0.01

* For site 6 phenolic resin production the PECaquatic could not be calculated and therefore no PEC/PNEC ratio could be established.

Conclusions to the risk assessment for the aquatic compartment (including sediment):

Conclusion (i) There is a need for further information and/or testing. This conclusion applies to endocrine disruption. Based on in vitro data on ptBP and read across from similar alkyl phenol compounds, including p-tert-pentylphenol, which have shown endocrine disrupting properties in vivo, it is concluded that further testing should be required for ptBP. As a "Tier 2 test" an Extended Early Life-Stage test on fish according to the draft OECD guideline will be performed.

Conclusion (i) applies to phenolic resin production site 6 where no site specific data is available and no PECaquatic could be derived. Further exposure information is needed in order to calculate a PECaquatic for this site.

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

This conclusion applies to the life-cycle steps production, for the production of phenolic resins, where site specific data are available, for sub-scenario 2 and 3 of the production of epoxy resins and for the production of polycarbonate resins.

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

This conclusion applies to the generic scenario for phenolic resin production (PEC/PNEC 28) and sub-scenarios 1 and 4 of the epoxy resin production (PEC/PNEC 121 and 30, respectively).

For production of phenolic resins site specific information has been obtained only for about 50 % of the total tonnage used in this use category. Therefore a generic scenario has been conducted which resulted in a risk to the aquatic compartment. The exposure assessment for the production of phenolic resins is based on an average emission factor obtained from the site having the highest emissions participating in the EPRA water monitoring program and on default parameters from the TGD. The size of the site has been chosen in close cooperation with industry. For the sites where site specific information is available no risk has been identified.

Concerning the production of epoxy resins no site specific data have been obtained by industry but only qualitative descriptions of the processes involved. No data on emissions to the environment has been obtained. The information resulted in four sub-scenarios, which have been proposed by industry. TGD default parameters have been used to calculate environmental concentrations. The TGD values have partly been adapted due to information from industry (sub-scenario 4).

Regarding the release from ambient cured epoxy products no further information on releases to the environemtn has become available.

More site specific information may give evidence of lower emissions than estimated in these two use categories, maybe resulting in no risk. However, no such data has been obtained despite of much effort that has been undertaken by the ptBP producers to obtain this information during the last 1 ½ years.

3.3.2.1 Marine risk assessment

In Table 3-3 risk characterisation is performed using a PNECmarine of 0.64 µg/l This is only a provisional assessment as there is a request to perform a chronic fish test that may change the aquatic PNEC. According to recent information from industry during the risk reduction phase site 5 , originally reported amongst the phenol/formaldehyde resin production sites, uses ptBP in the production of tri-aryl phosphate esters. The emission scenario had been considered to be comparable to the phenolic resins production scenarios. For two phenolic

resin production sites a marine risk assessment is carried out because these sites emit its treated waste water to a coastal zone (site 5 and 8).

Table 3-3: Estimated local PEC/PNECs for the aquatic compartment (including sediment)

Use category	Estimation method	PECaquatic/marine [µg/l]	PEC/PNEC
Phenolic resins	Site specific, site 5 , marine Site specific, site 8 marine	not stated as tonnage confidential < 0.02	**> 1** < 0.03
Regional PEC marine	TGD	0.009	0.01

Conclusion (i) applies to phenolic resin production site 5, where the PEC marine has been calculated using generic parameters and a risk has been identified. The exact value is not given as the tonnage used at this site is considered confidential. Further exposure information is needed in order to refine the PEC marine for this site.

Conclusion (ii) applies to phenolic resin production site 8. The local PEC marine for this site is below 0.02 µg/l. The PEC/PNEC ratio is below 0.03.

Conclusions ii) for the aquatic compartment has to be seen as provisional until possible endocrine effects in fish have been resolved.

3.3.2.2 Microorganisms in STP

A PNEC of 1.5 mg/l is established for effects on microorganisms in STP. In Table 3-4 the PEC/PNEC for the different use categories are shown.

Table 3-4: Estimated local PECs for the STP compartment. Only highest value estimated is presented for each use category.

Use category	PECSTP [mg/l]	PEC/PNEC
Production (site B)	0.02	0.01
Phenolic resins (water monitoring program)	≈ 0.01	0.007
Phenolic resins (site 8, LOD) (Site 5)[1] Phenolic resins (site 6)[2]	0.01 not stated as tonnage confidential - 	0.007 **> 1** **-**
Phenolic resins (TGD, generic scenario)	1.78	**1.2**
Polycarbonate resins, location A	0.0013	$8.7*10^{-4}$
Epoxy resins (TGD generic scenarios) Sub-scenario 1 Sub-scenario 2+3 Sub-scenario 4	 7.75 0.02 1.94	 **5.2** 0.01 **1.3**

1) For site 5 ptBP is used in the production of tri-aryl phosphate esters. The emission scenario is considered to be comparable to the phenolic resins production scenarios.
2) For site 6 phenolic resin production the PEC_{STP} could not be calculated and therefore no PEC/PNEC ratio could be established.

Conclusion (i) applies to phenolic resin production site 5, where the PEC_{STP} has been calculated using generic parameters and a risk has been identified. The exact value is not given as the tonnage used at this site is considered confidential. Further exposure information is needed in order to refine the PEC_{STP} for this site.

Conclusion (i) also applies to phenolic resin production site 6, where no site specific data is available and no PEC_{STP} could be derived. Further exposure information is needed in order to calculate the PEC_{STP} for this site.

Conclusion (ii) applies to sewage treatment plants for the production of ptBP, for the production of phenolic resins where site specific data are available, for sub-scenario 2 and 3 for the production of epoxy resins and for the production of polycarbonate resins.

Conclusion (iii) applies to the generic scenarios for phenolic resin production (PEC/PNEC 1.2) and sub-scenarios 1 and 4 of the epoxy resin production (PEC/PNEC 5.2 and 1.3, respectively).

3.3.3 Terrestrial compartment

The PNECsoil is 73 µg/kg wwt based on the equilibrium partitioning method. As indicated in Table 3-5 the two use categories phenolic and epoxy resins result in exposure to agricultural soil via sludge application.

Table 3-5: Estimated PEC for agricultural soil for scenarios estimated according to TGD default assessment

Use category	PECsoil [µg/kg] wwt	PEC/PNEC
Phenolic resins - generic	1,110	**15**
Epoxy resins - generic		
Sub-scenario 1	4,830	**66**
Sub-scenario 2+3	20	0.27
Sub-scenario 4	1,210	**17**

No risk characterisation for industrial soil has been carried out.

Conclusion (ii) This conclusion applies to the generic scenario for epoxy resin production sub-scenarios 2 and 3.

Conclusion ii) for the terrestrial compartment has to be seen as provisional until possible endocrine effects in fish have been resolved.

Conclusion (iii) This conclusion applies to the generic scenarios for phenolic resin production (PEC/PNEC 15) and sub-scenarios 1 and 4 of the epoxy resin production (PEC/PNEC 66 and 17, respectively).

3.3.4 Atmosphere

No risk assessment for the atmospheric compartment has been conducted.

Conclusion (ii) applies to atmospheric compartment. Although some release to air is reported for one production site and release to air is assumed using default release fractions in the TGD, the properties of ptBP indicate that this compound will rapidly degrade or be transferred to the aquatic compartment. No additional information is assumed necessary with respect to the air compartment.

3.3.5 Secondary poisoning

No risk assessment for secondary poisoning has been performed.
Conclusion (**ii)** available data indicate that ptBP is unlikely to bioaccumulate in the food chain. No further information is considered necessary.

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

The human population may be exposed to ptBP at the workplace, from the use of consumer products and indirectly via the environment.

4.1.1.1 Occupational exposure

Occupational exposure may find place during production of ptBP or when ptBP is used as a chemical intermediate when plastic polymers (polycarbonate, phenolic or epoxy resins) are produced. End use of the products containing resins (paints, glues) may also give rise to exposure. The main routes of exposure for workers are expected to be by inhalation and skin contact.

The following scenarios are considered for occupational exposure to ptBP:

Scenario I: Production of ptBP;
Scenario II: Users of ptBP as an intermediate (formulation and processing)

- phenolic resins producer
- polycarbonate producer
- epoxy resins producer
- producer of chemicals used in synthesis.

Scenario III: Professional end uses as for example use of resins and paints.

Table 4-1 summarizes the exposure data carried forward to the risk characterisation for workers. For scenarios where there are few available measurements or no measurements at all, modelled data are used.

Table 4-1: Conclusions of occupational exposure

Scenario	Activity [1]	Frequency Days/year	Duration Hours/day	Inhalation				Dermal			
				Reasonable worst case		Typical concentration		Reasonable worst case		Typical concentration	
				Unit mg/m³	Method[2]	Unit mg/m³	Method [2]	Unit mg/day	Method [2]	Unit	Method [2]
Sc 1 Production											
Production Operators											
Product packing	Full shift	Every day	8h/ pr day	0.76	Measured	0.39	Measured	Negligible Automated system			
Sampling	Short term	6X1min a day		19	EASE	7.3	Measured	Negligible (hot liq.)			
Sc 2 Formulation and Processing											
II.1 Production of polycarbonate resins											
Production	Full shift		8h/day	0.014	Measured			Negligible (hot liq.)			
operators											
Unloading ptBP from ISO tanks	Short Term	2-3 times a week	1-1.5 h/day	0.6	EASE	0.11	Measured	Negligible (hot liq.)			
II.2 Production of phenolic resins, Production of chemicals used in synthesis											
Production	Full shift		8h/day	0.6	EASE			Negligible (hot liq.)			
II.3 Production of epoxy resins											
Formulation		1 h /day		6.6	Measured, personal			420	EASE		
Sc 3 End use scenarios											
III.1 Use of	Full time			< 0.01	Measured			Negligible			

polycarbonate								(hot liq.)			
III.2 Use of phenolic resin. Handling uncured glue	Full time	Every day		12	EASE dilution			33.6	Default value, dilution		
III.2 Use of phenolic resins. Spray painting.	Full time	Every day		2.4	TNO			50	TGD Appendix 1E		
III.3 Use of epoxy resin. Manually handling of reactants	Full time	Every day		93	EASE dilution			510	Default value, dilution		
III.3 Use of epoxy resins. Tank spraying.	Full time	Every day		5.6	TNO			3600	Default value, Marquart	1020	Default value, Marquart
III.4 Use of rubber addiitive in uncured rubber	Full time	Every day		0.09	EASE dilution			0.13	EASE, dilution		

4.1.1.2 Consumer exposure

Potential consumer exposure is via direct use of products with phenolic resins or epoxy resins containing residual ptBP monomers, or via use of the final product containing residual concentration of ptBP. The main exposure from final products is expected to be from adhesives and possibly canned food. Consumers may also be exposed to ptBP in drinking water from drinking water reservoirs coated with epoxy-based paints or from pipelines. Consumers may moreover be exposed to ptBP from polycarbonate used for food contact material. The main routes of exposure to consumer products are by dermal contact (e.g. use of adhesives) and by ingestion of food products into which ptBP have migrated from the food/water container or packaging (e.g. food contact applications), Table 4-2

The following scenarios are considered for consumer exposure to ptBP:

I. Exposure from direct consumer use of adhesives containing ptBP

II. Exposure to ptBP in drinking water from drinking water reservoirs and pipelines

III. Exposure to ptBP from polycarbonate used for food contact applications

IV. Exposure to ptBP from epoxy resins used for canned food

Table 4-2: Summary of consumer exposure (external exposure)

Exposure scenario	Dermal µg/kg bw/day	Oral µg/ kg bw/day
Ii Exposure from direct consumer use of adhesives (superglue) containing ptBP	0.051	
Iii Exposure from direct consumer use of adhesives (Universal glue) containing ptBP	20.3[6]	
II Exposure to ptBP in drinking water from drinking water reservoirs		0.0057
II Exposure to ptBP in drinking water from pipelines		0.027
III Exposure to ptBP from polycarbonate used for food contact applications		0.23
IV Exposure to ptBP from epoxy resins used for canned food		0.71

4.1.1.3 Humans exposed via the environment

For humans exposed indirectly via the environment, the main exposure is expected to be from ingestion.

[6] 0.142 mg/kg bw/event

The daily human intake via the environment based upon typical human consumption and inhalation rates at the regional level is 2.7 x 10^{-5} mg/kg bw/day, and the highest local exposure scenario (epoxy resin production) is 0.073 mg/kg bw/day.

4.1.1.4 Combined exposure

Humans may be exposed to ptBP as workers, consumers or via the environment. However, since occupational exposure values will totally dominate the exposure levels it is not considered relevant to make a separate calculation for combined exposure including occupational exposure. In Table 4-3 the combined local and regional exposure to ptBP is given

Table 4-3: Combined consumer exposure and regional and local exposure to ptBPb (occupational exposure to ptBP not included)

Scenario	Daily intake mg/kg bw/day
Ii Adhesives containing ptBP (super glue)	0.000051
Iii Adhesives containing ptBP (universal glue)	0.0203
II Drinking water reservoirs and pipelines	0.000033
III Polycarbonate used for food contact applications	0.00023
IV Epoxy resins used for canned food	0.00071
Local exposure[a]	0.073
Regional exposure	0.000027
Combined locala	0.074c/0.094d
Combined regional	0.0011c/0.0211d

[a] Highest excposure scenario for local exposure (epoxy resin production)
[b] Workers: Inhalation exposure (internal) at production: epoxy resins 0.94 mg/kg/day; phenolic resins 0.09 mg/kg/day. End use: epoxy resins 13.3 mg/kg/day; Phenolic resins 1.7 mg/kg/day
[c] Included scenario Ii.
[d] Included scenario Iii.

4.1.2 Effect assessment

Toxicokinetics, metabolism and distribution

No data from toxicokinetic studies according to OECD guideline 417 are available. However, the role of sulfatation and glucuronidation in the biotransformation of ptBP was assessed in vivo in rats as well as in vitro in rats and humans.

The excretion of ptBP via feces and urine was assessed in rats exposed to ptBP by the oral route. The results showed that 26.7% and 72.9% of the applied dose were eliminated via feces and urine, respectively. In another in vivo rat study where ptBP was injected intravenously 65 – 71% and 17 – 21% of the intravenously applied dose were excreted as glucuronide and sulphate conjungates, respectively. The total recovery of radioactivity was 91 – 93 %. The in

vitro studies with rat hepatocytes and the human liver supported the results of the in vivo rat study with intravenoulsy applied ptBP. The results of the rat studies where the retention of ptBP after 7 days was 0.1% can be regarded as negligible, and the likelihood for bioaccumulation is low.

The urinary metabolite levels in workers handling ptBP showed an increasing level of ptBP metabolites in the urine with increasing exposure to ptBP. Most of the ptBP was shown to be excreted within 24 hours. The studies indicated that skin penetration plays an important role as a route of entry in addition to inhalation.

In a study on rats, 26.7% and 72.9% of the orally applied dose were eliminated via feces and urine, respectively. In this study there was no information whether the faeces derived radioactivity stems from metabolites or unabsorbed ptBP. However, in another study nearly 100 % of the intravenous applied dose was excreted as conjugated metabolites in urine and bile in rats.

Based on available data and using the criteria in the TGD, 100 % absorption is assumed following inhalation, dermal and oral exposure to ptBP in the risk characterisation.

Acute toxicity

PtBP appears to have low acute toxicity following inhalation, dermal and oral exposure. In rats in a limit test the LC_{50} value via inhalation was above 5600 mg/m^3 (dust aerosol, with an additional vapour component of 30 mg/m^3). Most studies show dermal and oral LD_{50} values above 2000 mg/kg bw. The exception is an oral rat study with an LD_{50} of 801 mg/kg bw. In this study the increasing volumes of DMSO used for intubation of increasing doses of ptBP may be an explanation of the elevated acute toxicity observed in this study compared to the other acute oral toxicity studies reported. The available studies fulfil the Annex VIIA test requirements for evaluation of acute toxicity.

Irritation

No studies in humans were located. In animals ptBP is shown to be moderately to severely irritating to skin and the respiratory system. PtBP may cause serious damage to eyes.

Five skin irritation studies in rabbits were identified. PtBP was irritating and severely irritating in the two studies performed according to tests fulfilling the Annex VIIA requirements for irritation. PtBP was skin irritating in the three other tests as well but even some case of skin corrosion were reported. PtBP was highly irritating to eyes inducing corneal opacity, iris lesion and chemosis in two studies in rabbits. Mucosal irritation and respiratory irritation seen as respiratory distress (audible respiration gasping and and decreased respiration rate) were seen in the acute inhalation toxicity study (limit test) in rats.

Corrosivity

Two studies have reported the occurrence of skin necrosis in a minority of animals following 4 hour exposure.

Sensitisation

Of the three animal studies on skin sensitisation reported, two is negative and one is positive. The negative studies use the Guinea Pig Maximization test and have been performed according to current test guidelines and GLP. The positive study is an older study and the protocol is not well described. No firm conclusions can be drawn based on the animal studies.

There are several sensibilisation studies performed using patch tests of patients with either work related contact allergy or general allergy. Furthermore, many case reports were found in the literature. Many of them used ptBP-FR and are of limited value in evaluating a possible sensitisation potential for ptBP. The results from these studies/reports give a very variable picture of human sensitisation to ptBP. The database for assessing skin sensitisation for ptBP has limitations. The animal data are of varying reliability and are not sufficient to draw any conclusions of ptBP as a sensitiser. The human data are also of limited value since most of the studies shows very few positive results and they are mainly performed on patients with former skin allergy or other skin deseases or there is limited information about the exposure substance. PtBP does not fulfil the classification criteria for skin sensitisers according to the Technical Committee on Classification and Labelling.

Repeated dose toxicity

There are no studies of repeated dose toxicity after inhalation or dermal exposure. The evaluation is based on a combined test (repeated dose and reproductive/developmental screening) and a two-generation reproduction study, both in rats. A systemic NOAEL of 70 mg/kg bw/day for repeated dose toxicity was established from a two-generation reproduction study with oral administration in albino rats. The study was performed according to OECD Guideline 416 (Clubb and Jardine, 2006). There was a dose-dependent reduction in relative organ weights. This NOAEL was used for all scenarios in the risk characterisation except for depigmentation (due to the use of albino rats not suitable for detection of depigmentation). Effects on reproduction is summarized below.

Skin depigmentation has been reported in workers in factories manufacturing/handling ptBP and ptBP-formaldehyde resin (ptBP-FR) but the available human studies are of low quality. However, there is a depigmentation study with a single dose level performed on C57 black mice dosed orally three times a week for six months (Hara and Nakajima, 1969). This study is the basis for a systemic LOAEL of 103 mg/kg/day. There are many other studies using black animals describing systemic skin depigmentation after various administrations routes. There are also guinea pig studies describing local skin depigmentation after skin contact with ptBP.

Mutagenicity

A variety of *in vitro* and *in vivo* genotoxicity studies are available for ptBP. PtBP showed no evidence of mutagenicity in tests with *Salmonella typhimurium* or *E.Coli*. The mouse lymphoma TK+/-locus assays have given both negative and positive results, apparently depending upon duration of exposure. PtBP induced chromosomal aberrations with an exogenous metabolic activation and polyploidy with and without an exogenous metabolic activation in two studies with Chinese hamster lung cells but not in a study with rat lymphocytes. Thus, the overall results regarding mammalian cell mutagenicity *in vitro* is inconclusive.

To elucidate *in vivo* genotoxicity of ptBP, a mammalian erythrocyte micronucleus test was conducted. No increase in the frequency of micronucleated bone marrow cells was observed in any dose group. It is considered likely that the material had reached the target organ. Based on data from the other alkylphenols and the mutagenicity data on ptBP available, it is assumed that ptBP most likely is not mutagenic.

Carcinogenicity

The database for assessing carcinogencitiy is limited, and the studies´ duration is too short to draw firm conclusions. Single intragastric dosing of PtBP followed by exposure through the diet for 51 weeks induced forestomach squamous cell carcinoma after initiation with MNNG in rats and forestomach hyperplasia in uninitiated rats. The hyperplasia was probably due to ptBPs irritating effect. Forestomach hyperplasia was also seen in hamsters receiving ptBP through the diet for 20 weeks. No conclusions regarding ptBP could be drawn from a population-based case-control study. Most probably the mechanism of ptBP induction of forestomach tumours is the promotor effect. The induction of forestomach tumours in rodents by agents without demonstrable genotoxicity may be of little relevance to humans, according to IARC. The available studies on carcinogenicity are not sufficient to assess to carcinogenic potential of ptBP, but as ptBP is most likely not mutagenic, it is unlikely that the substance is carcinogenic.

Toxicity for reproduction

The studies available are a recent OECD 416 two-generation reproduction toxicity study and an OECD 422 Combined Repeated Dose and Reproductive/Developmental Toxicity Screening Test. The results from the Combined Repeated Dose and Reproductive/Developmental Toxicity Screening Test (OECD 422) indicated that ptBP had no effect on fertility and induced no embryotoxicity or teratogenicity at the dose levels tested (0, 20, 60 and 200 mg/kg bw/day). The NOAEL for fertility and developmental toxicity derived from this study was ≥ 200 mg/kg bw/day.

Based on the available data on fertility/effects on the reproductive organs a NOAEL of 70 mg/kg bw/day was derived from a 2-generation reproduciton toxicity study in rats. The NOAEL value was based on an increase in vaginal epithelium atrophy and decreased ovary weight accompanied with a slight reduction in implantation sites.

For developmental effects a NOAEL at 70 mg/kg bw/day was derived from a 2-generation reproduciton toxicity study in rats. The NOAEL was based on a decrease in foetal body weights in the F1 and F2 generation. In in vitro studies ptBP was shown to have a weak estrogenic activity. A possible anti-androgen activity of ptBP has not been elucidated.

4.1.3 Risk characterisation

In the risk characterisation, 100% absorption is used for oral exposure. This is based on the study by Freitag et al., where 26.7% and 72.9% of the orally applied dose were eliminated via feces and urine, respectively. In this study there was no information whether the faeces derived radioactivity stems from metabolites or unabsorbed ptBP. However, in the study by Koster et al., 1981 nearly 100 % of the intravenous applied dose was excreted as conjugated metabolites. Absorption of nearly 100 % is expected since ptBP has a low molecular weight

(152), low Kow value (3.31) and high solubility in water (600 mg/l). In the absence of data on the percentage absorption by inhalation, a default value of 100 % is used for inhalation exposure. For dermal exposure no studies are available. However, related to the water solubility (600 mg/l), a $logP_{ow}$ value at 3.31 and low molecular weight (152) for ptBP dermal absorption of 100% is assumed (according to the criteria in the TGD).

4.1.3.1 Workers

The main routes of exposure for workers are expected to be by inhalation and dermal contact.

Acute toxicity

PtBP appears to have low acute toxicity by all exposure routes. A limit test gives an LC_{50} for inhalation above 5600 mg/m^3 (dust aerosol) with an additional vapour component of 30 mg/m^3. Most studies report dermal and oral LD_{50} values above 2000 mg/kg bw. The exception is an oral acute toxicity study where high and increasing doses of vehicle (DMSO) is likely to have influenced the toxicity reported.

Compared with the anticipated occupational exposure levels from inhalation and dermal contact, it is concluded that ptBP is of no concern for workers in all exposure scenarios with respect to acute effects (conclusion ii).

Irritation and corrosivity

PtBP is regarded as severely irritating to skin, eyes and the respiratory system. Corrosive effects have also been reported. In addition PtBP may induce partial depigmentation of the skin. No threshold level has been identified for irritation of the skin, eyes or respiratory tract. The COM WG on classification and labelling has agreed on classification of ptBP as an irritant. Due to this and to the assumption that personal protective equipment is regularly worn by workers as stated by industry, conclusion ii) is drawn for all occupational scenarios.

Sensitisation

The database for assessing skin sensitisation has limitations. The human studies have major limitations in both number of test samples and mainly that the patients were suffering from former skin allergy or other skin diseases. Also the animal data are of varying reliability and the conclusion is drawn that ptBP does not fulfill the classification criteria as a sensitizer (conclusion ii).

Repeated dose toxicity

The risk characterisation for repeated dose toxicity is discussed both for repeated dose toxicity in general and for (skin) depigmentation as the assessment of these endpoints rest upon two different animal studies. For general endpoints a NOAEL of 70 mg/kg bw/day was concluded from a 2-generation reproduction toxicity study in Sprague-Dawley rats. For skin depigmentation as a systemic effect following oral administration in mice a LOAEL was calculated to be 103 mg/kg bw/day.

For general endpoints a minimal MOS value was calculated to be 50 (interspecies differences 10, intraspecies differences 5). For skin depigmentation as a systemic effect a minimal MOS value was calculated to be 525 (17.5 interspecies differences, 5 intraspecies differences, differences in duration of exposure 2, dose-response relationship 3).

Table 4-4 and Table 4-5 give an overview of the conclusions.

Table 4-4:Occupational risk assessment for repeated dose toxicity, general systemic (min MOS = 50). NOAEL is 70 mg/kg bw/day (Clubb and Jardine, 2006)

Scenario	Internal combined exposure (mg/kg bw/day) (with PPE*)	MOS	Conclusion (with PPE*)
Scenario I: Production of ptBP			
Product packers (highest measured TWA-value)	0.11	636	ii
Typical concentration	0.056	1250	ii
Short term (both RWC and typical)	negligible	-	ii
Scenario II: Formulation and processing			
Subscenario 1 Production of polycarbonate resins	0.002	35000	ii
RWC Short term	0.011	6363	ii
Subscenario 2 Production of phenolic resins	0.09	778	ii
Subscenario 3 Production of epoxy resins (1 h/day)	6.12 (0.72)	11.4 (97)	iii ii
Scenario III: Professional end-use of products containing ptBP			
Subscenario 1 Use of polycarbonate	0.001	70000	ii
Subscenario 2 Use of phenolic resin Spray painting	2.18 (1.7) 1.04 (0.41)	32.1 (40.0) 67.3 170.7	iii (iii) ii (ii)
Subscenario 3 Use of epoxy resin Tank spraying, RWC	20.6 (14) 52.2 (5.9)	3.4 (5) 1.3 (11.9)	iii (iii) iii (iii)
Tank spraying, typical concentration	15.4 (1.54)	4.5 (0.45)	iii (iii)
Subscenario 4 Use of rubber additive	0.012 (0.01)	5833 (7000)	ii (ii)

*i.e. the assumption that 90 % of the substance is prevented to reach the skin due to use of gloves. These reduced values are only given for scenarios with non-negligible dermal exposure

Table 4-5: Occupational risk assessment for repeated dose toxicity, depigmentation (min MOS = 525). LOAEL is 103 mg/kg bw/day (Hara and Nakajima, 1969)

Scenario	Internal combined exposure (mg/kg bw/day) (with PPE*)	MOS	Conclusion (with PPE*)
Scenario I: Production of ptBP			
Product packers (highest measured TWA-value)	0.11	936	ii
Typical concentration	0.056	1839	ii
Short term (both RWC and typical)	negligible	-	ii
Scenario II: Formulation and processing			
Subscenario 1 Production of polycarbonate resins	0.002	51500	ii
RWC Short term	0.011	9363	ii
Subscenario 2 Production of phenolic resins	0.09	1144	ii
Subscenario 3 Production of epoxy resins (1 h/day)	6.12 (0.72)	16.8 (143)	iii (iii)
Scenario III: Professional end-use of products containing ptBP			
Subscenario 1 Use of polycarbonate	0.001	103000	ii
Subscenario 2 Use of phenolic resin Spray painting	2.18 (1.7) 1.04 (0.41)	47.2 (60.6) 99 (251)	iii (iii) iii (iii)
Subscenario 3 Use of epoxy resin Tank spraying, RWC	20.6 (14) 52.2 (5.9)	5 (7.4) 2 (17.5)	iii (iii) iii (iii)
Tank spraying, typical concentration	15.4 (1.54)	6.7 (45.6)	iii (iii)
Subscenario 4 Use of rubber additive	0.012 (0.01)	8583 (10300)	ii (ii)

*i.e. the assumption that 90 % of the substance is prevented to reach the skin due to use of gloves. These reduced values are only given for scenarios with non-negligible dermal exposure

Mutagenicity
Based on the available data ptBP does not fulfil the criteria for classification as mutagenic. A conlusion ii is drawn for all scenarios.

Carcinogenicity
It is considered unlikely that ptBP should be a human carcinogen. However, its ability to increase the frequency of squamous cell carcinomas in the rat forestomach following initiation with MNNG indicates that ptBP may act as a tumour promoter in rats. The available studies on carcinogenicity are not sufficient to assess to carcinogenic potential of ptBP, but as ptBP most probably is not mutagenic; it is unlikely that the substance is carcinogenic. A conclusion ii is drawn for all scenarios.

Toxicity for reproduction
A NOAEL 70 mg/kg bw/day was concluded from a 2-generation study in Sprague-Dawley rats. This value is used in the risk characterisation for reproduction, both fertility and developmental.

Fertility
The calculated MOS values for fertility will be the same as those given for repeated dose toxicity in Table 4-4 Also the same uncertainties factors will be used as for repeated dose toxicity and a min MOS = 50.

A conclusion iii is drawn for

- II.3 Formulation and processing, Production of epoxy resins (dermal without PPE), (combined without PPE)
- III.2 End uses, Use of phenolic resins (inhalation) (combined, with and without PPE)
- III.3 End uses, Use of epoxy resins (inhalation) (dermal without PPE) (combined, with and without PPE)
- III.3 End uses, Use of epoxy resins, tank spraying (RWC): (dermal, with and without PPE) (combined, with and without PPE)
- III.3 End uses, Use of epoxy resins, tank spraying (typical conc): (dermal, with and without PPE) (combined, with and without PPE)

Development

The calculated MOS values for developmental toxicity will be the same as those given for repeated dose toxicity in Table 4-4. For development a minimal MOS value was calculated to be 100 (interspecies differences 10, intraspecies differences 10 (there will be made no distinction between the progeny of the occupational population and the general population)). For skin depigmentation as a systemic effect a minimal MOS value was calculated to be 525 (17.5 interspecies differences, 5 intraspecies differences, differences in duration of exposure 2, dose-response relationship 3).

The min MOS value is compared with the MOS values given in Table 4-4 for repeated dose toxicity. *In addition* to the scenarios in Table 4-4 with concern and concl iii), the following scenarios with MOS in the range 50 – 100 will also give conclusion iii) for development:

- II.3 Formulation and processing, Production of epoxy resins (dermal without PPE), (combined with and without PPE)

- III.2 End uses, Use of phenolic resins (inhalation) (combined, with and without PPE)
- III.2 End uses, Use of phenolic resins, spray painting (combined, with and without PPE)
- III.3 End uses, Use of epoxy resins (inhalation) (dermal with and without PPE) (combined, with and without PPE)
- III.3 End uses, Use of epoxy resins, tank spraying (RWC): (inhalation) (dermal, with and without PPE) (combined, with and without PPE)
- III.3 End uses, Use of epoxy resins, tank spraying (typical conc): (inhalation) (dermal, with and without PPE) (combined, with and without PPE)

Consumers

For consumer exposure four main exposure scenarios have been identified:

I. Exposure from direct consumer use of adhesives containing ptBP

II. Exposure to ptBP in drinking water from drinking water reservoirs and pipelines

III. Exposure to ptBP from polycarbonate used for food contact applications

IV. Exposure to ptBP from epoxy resins used for canned food

In the calculation of the internal exposure to ptBP 100 % absorption is assumed for oral, dermal and inhalation exposure.The MOS values for the different endpoints assessed with NOAEL or LOAEL values are presented in Table 4-7.

In table 4-8 the conclusions for the consumer exposure scenarios are presented. Conclusion ii) is derived for all consumer exposure scenarios for all endpoints. This also applies to endpoints where no NOAEL/LOAEL values are established (irritation, corrosivity, sensitisation, mutagenicity and carcinogenicity).

Table 4-6: Derived N(L)OAEL values

Endpoint	NOAEL mg/kg bw/day	LOAEL mg/kg bw/day
Acute toxicity		2000
Repeated dose toxicity	70	
Reproductive toxicity	70	
Skin depigmentation (RDT)		103

Table 4-7: MOS values for the four consumer scenarios

Scenarios/Endpoint	**scenario Ii**	**scenario Iii**	**scenario II**	**scenario III**	**scenario IV**
Acute toxicity	5555600	14100			
Repeated dose toxicity (RDT)	1370 000	3500	12300000[a]	300 000	99 000

			2600 000[b]		
Skin depigmentation (RDT)	2019608	5150	18070200[a] 3820000[b]	448000	145000
Reproductive toxicity	1370 000	3500	12300000[a] 2600 000[b]	300 0000	99 000

[a]Exposure to ptBP in drinking water from drinking water reservoirs

[b]Exposure to ptBP in drinking water from pipelines

The minimal MOS value for acute toxicity was calculated to 300 (interspecies differences 10, intraspecies differences 10, dose-response relationship 3), for repeated dose toxicity 100 (interspecies differences 10, intraspecies differences 10), for depigmentation 1050 (interspecies differences 17.5, intraspecies differences 10, differences in duration of exposure 2, dose-response relationship 3) and for reproductive toxicity 100 (interspecies differences 10, intraspecies differences 10).

Table 4-8: Conclusions for the four consumer exposure scenarios

Endpoint	**Conclusion scenario I**	**Conclusion scenario II**	**Conclusion scenario III**	**Conclusion scenario IV**
Acute toxicity	ii/ii (scenario Ii/ scenario Iii)	ii	ii	ii
Irritation/corrosivity skin	ii			
Irritation eye	ii			
Corrosivity	ii			
Sensitisation	ii			
Repeated dose toxicity	ii/ii (scenario Ii/ scenario Iii)	ii	ii	ii
Depigmentation	ii/ ii (scenario Ii/ scenario Iii)	ii	ii	ii
Mutagenicity	ii	ii	ii	ii
Carcinogenicity	ii	ii	ii	ii
Reproductive toxicity	ii/ ii (scenario Ii/ scenario Iii)	ii	ii	ii

Humans exposed via the environment

The endpoints associated with exposure to ptBP via the environment are repeated dose toxicity, mutagenicity, carcinogenicity and reproductive toxicity including both effects on fertility in adults and developmental effects in offspring.

Table 4-9: MOS values for indirect human regional and local exposure to ptBP via the environment

Scenario[a]	Human intake mg/kg bw/day	MOS repeated dose toxicity[b]	MOS RDT, depigmentation[c]	MOS fertility/development[b]
Regional exposure	2.7×10^{-5}	2600 000	3800000	2600 000
Local exposure	0.073	960	1400	960

[a]Referes to the scenarios described in section 3.1.1

[b]NOAELvalue (70 mg/kg/day) from an oral 2-generation reproduction toxicity study in rats (Clubb and Jardine, 2006).

[c] LOAEL (103 mg/kg/day) value from an oral exposure depigmentation study in mice (Hara and Nakajima, 1969).

Table 4-10: Summary of the conclusions for humans exposed via the environment

Critical endpoint	Local exposure[a]	Regional exposure[b]
Repeated dose toxicity	ii	ii
RDT, depigmentation	ii	ii
Mutagenicity	ii	ii
Carcinogenicity	ii	ii
Reproductive toxicity	ii	ii

[a]Highest indirect local exposure (production of epoxy resins) as estimated by EUSES (0.073).

[b]Indirect regional exposure as estimated by EUSES

Regarding combined exposure where humans are exposed to ptBP both as consumers and via the environment, conclusion ii) is drawn for all endpoints. For workers who are exposed to ptBP both occupationally and as consumers and via the environment the occupational exposure values will totally dominate the exposure levels. Because of this it is not considered relevant to make a separate calculation for combined exposure including occupational exposure

5 OVERALL RESULTS OF THE RISK ASSESSMENT

5.1 ENVIRONMENT

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

Conclusion (i) applies to endocrine disruption. Based on *in vitro* data on ptBP and read across from similar alkyl phenol compounds, including p-tert-pentylphenol, which have shown endocrine disrupting properties *in vivo*, it is concluded that further testing should be required for ptBP. As a "Tier 2 test" an Extended Early Life-Stage test on fish according to the draft OECD guideline will be performed.

Conclusion (i) applies to phenolic resin production site 5, where the PEC_{marine} as well as the PEC_{STP} have been calculated using generic parameters and a risk to the marine environment and to microorganisms in the WWTP has been identified. The exact values for the PEC/PNEC ratios are not given as the tonnage used at this site is considered confidential. Further exposure information is needed in order to refine the the PEC_{marine} and the PEC_{STP} for this site.

Conclusion (i) applies to phenolic resin production site 6 where no site specific data is available. No $PEC_{aquatic}$ and no PEC_{STP} could be derived and therefore no risk assessment for the aquatic compartment and for microorganisms in the WWTP has been carried out. Further exposure information is needed in order to calculate a $PEC_{aquatic}$ and a PEC_{STP} for this site.

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

Conclusion (ii) applies to the life-cycle steps production, to the production of phenolic resins, where site specific data are available, for the generic sub-scenario 2 and 3 of the production of epoxy resins and to the production of polycarbonate resins for all environmental compartments.

Conclusion (ii) applies to phenolic resin production site 8 for the marine environment. The PEC/PNEC ratio for the marine environment is below 0.03.

According to information from industry no emissions to the environment are expected from the use of ptBP in the production of oilfield chemicals and the scenario "Hydrogenation" and therefore conclusion (ii) applies.

No risk assessment for secondary poisoning has been performed. Available data indicate that ptBP is unlikely to bioaccumulatein the food chain. No further information is considered necessary.

Conclusions ii) for the aquatic and the terrestrial compartment have to be seen as provisional until possible endocrine effects in fish have been resolved

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account

Conclusion (iii) applies to the generic scenario for phenolic resin production and to the generic sub-scenarios 1 and 4 of the epoxy resin production for the aquatic compartment (including sediment). The PEC/PNEC ratios for phenolic resin production and for sub-scenarios 1 and 4 of the epoxy resin production are 28, 121 and 30, respectively.

Conclusion (iii) also applies to the generic scenario for phenolic resin production and to the generic sub-scenarios 1 and 4 of the epoxy resin production for the terrestrial compartment (PEC/PNEC ratios 15, 66 and 17, respectively) and for microorganisms in WWTPs (PEC/PNEC ratios 1.2, 5.2 and 1.3, respectively).

For production of phenolic resins site specific information has been obtained only for about 50 % of the total tonnage used in this use category. Therefore a generic scenario has been conducted which resulted in a risk to the aquatic and the terrestrial compartment, as well as to microorganisms in WWTPs. The exposure assessment for the production of phenolic resins is based on an average emission factor obtained from the site having the highest emissions participating in the EPRA water monitoring program and on default parameters from the TGD. The size of the site has been chosen in close cooperation with industry.

Concerning the production of epoxy resins no site specific data has been obtained by industry but only qualitative descriptions of the processes involved. No site-specific data on emissions to the environment has been obtained. The information received resulted in four sub-scenarios, which have been proposed by industry. TGD default parameters have been used to calculate environmental concentrations. The TGD values have partly been adapted due to information from industry (sub-scenario 4).

Regarding the release from ambient cured epoxy products no further information on releases to the environment has become available.

More site specific information may give evidence of lower emissions than estimated in the generic scenarios of the use categories “phenolic resins” and “epoxy resins”, maybe resulting in no risk. However, no such data could be made available despite of much effort that has been undertaken by the ptBP producers to obtain this information during the last 1 ½ years.

5.2 HUMAN HEALTH:

5.2.1 Workers

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

Conclusion (ii) applies to the endpoints acute toxicity, irritation, sensitisation, mutagenicity and carcinogenicity for all scenarios.

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

Conclusion (iii) applies to the endpoints of repeated dose toxicity and reproductive toxicity after dermal exposure arising from formulation and processing (production of epoxy resins)

and after inhalation and dermal exposure arising from end use of phenolic resins and end use of epoxy resins. Conclusion (ii) is reached for all other endpoints and scenarios.

5.2.2 Consumers

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

Conclusion (ii) applies to all scenarios and endpoints for consumers.

5.2.3 Humans exposed via the environment

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

Conclusion (ii) applies to all scenarios and endpoints for humans exposed via the environment.

5.2.4 Combined exposure

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

Conclusion (ii) applies to all scenarios and endpoints for combined exposure. Combined exposure is described as exposure to humans as consumers and via the environment. For humans exposed both in the working environment as well as consumers or indirect via the environment, the occupational exposure will exceed the other exposure sources by far, so it has not been considered relevant to assess combined exposure including workers.

5.3 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

PtBP has low vapour pressure. No data is available for flammability. The substance is reported to be combustible. The flash point is about 115°C. The chemical structure of this compound does not suggest a likelihood of explosivity or oxidizing properties. The risks from physicochemical properties are of no concern to either subpopulation (workers, consumers or humans exposed via the environment).

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

Conclusion (ii) applies to all scenarios